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THE PERIODIC LAW OF D. I. MENDELEEV AS A BASIC CONCEPT IN MODERN CHEMISTRY

(On the 85th Anniversary of the Discovery of the Law)

S. A. Shchukarev

D. I. Mendeleev wrote [1]: "Periodic relations belong to elements and not to simple bodies, and it is very important that one taken heed of this; . . . the physical properties are determined for the most part by the properties of the particles, and depend only indirectly upon the properties of the atoms which go to make up the particles. Because of this fact, periods which are clearly and distinctly expressed, for example in the form of compounds, are already complicated in their physical properties.

"The properties of simple and of complex bodies are in periodic relation to the atomic weights of the elements only for the reason that the properties of simple and of complex bodies are themselves the results of the properties of the elements which make them up."

It is now clear that the main periodicity in properties of uncombined atoms, which depends upon properties of the electrons and their interactions with one another and with the atomic nucleus, is further complicated by formation of molecules and condensed phases as the result of chemical bond formation, as well as by the effects of quantum-statistical and thermodynamic factors. However, despite such complication, there is evident in an overwhelming majority of cases, most clearly, and with utmost surety, a periodic law for the properties of chemical compounds.

Back in 1871, D. I. Mendeleev, in the conclusion of his first edition of "Principles of Chemistry", wrote: "A major concern of chemistry is a study of the basic properties of the elements, since their properties are not completely known to us, and since up till now we have developed precise knowledge of but two . . . measurable properties, namely, the ability to produce known types of compounds, and that property known as the weight of an atom, which, therefore, leaves but one route open for development of extensive knowledge of the elements, which is a comparative study of the elements based upon the two-mentioned properties."

The present position of science has changed, in relation to which fact, teaching of the Periodic Law has acquired a new development and application; in particular, a knowledge of spectral and ionization studies for an overwhelming majority of the elements in connection with formulas for electronic configurations of neutral and charged atoms, gives such a meaningful and profound picture of periodicity in properties of electronic shells, that such picture ought to be given priority in contrasting chemical compounds with respect to primary aspects of the Periodic Law.

In substance, the condition is dependent upon the partner (oxygen, hydrogen), and in individual cases even appears to be thermodynamically unstable (MgH_2, AlH_3, Bi_2O_5, F_2O_7), and hardly characteristic for the given element (K_2O), or failing to correspond to the group number (Fe_2O_3, NiO, etc.); it is, therefore, natural to look for identical characteristics for an external electronic layer in free (neutral and charged) atoms with respect to both normal electronic configurations for the element and with respect to activated values connected with such configurations.

By no means is there an opportunity in the present article to discuss systematically and fully even the most fundamental concepts of the problem of spectral-therm periodicity, and so we shall limit ourselves to an examination of only one problem which is of interest to chemists, namely, certain characteristics of periodicity of the principal ionization potentials of elements as related to the so-called secondary periodicity of heats of formation of binary chemical compounds. Thus, we shall illustrate a profound thought of D. I. Mendeleev regarding the transition from Periodic Law which characterizes the system of elements to the laws of chemical compounds.

Under the term secondary periodicity of ionization potentials we shall agree to include the following type of phenomena. It is known that in the fourth period of the system, the transition from K to Cu and from Ca to Zn correspond in first ionization potential to 3.4 and 3.1 eV; such increases depend upon the fact that the 4s- and $4s^2$-electrons drop into the more completely filled screen of 3d-electrons which are equivalent to each other, as the

result of which the effective nuclear charge increases,which attracts the external electrons of the atoms.

For the fifth period, transitions from Rb to Ag and from Sr to Cd, for similar reasons, produce an increase in ionization potential of 3.4 and 3.3 eV, respectively; however, sixth period transitions from Cs to Au and from Ba to Hg correspond to considerably larger increases, namely, 5.36 and 5.2 eV, because in this case the $6s^2$-electrons drop not only into the 5d-screen, but also into the 4f-screen consisting of 14 electrons.

The elements prior to the lanthanides, and particularly the series from Hf to Hg, do not possess particularly large ionization potentials, according to the picture presented.

Strengthening of s-electron bonds, which depends upon dropping into the d- and f-orbitals, is the basis for that difference which we see in the properties of both sub-groups of the first and second groups of the system.

Thus, primary ionization potentials for Cu and Zn exceed considerably the K and Ca potentials; the primary potentials for Ag and Cd on the other hand, are somewhat smaller than the primary potentials of Cu and Zn, due to an increase in the principal quantum-number for the s-electrons torn off. Transition from Ag and Cd to Au and Ag again leads to an increase in primary potential because of additional f-consolidation.

Thus appears an important development of a non-repetitive order of primary potentials for the series:

I group Li, Na, Cu, Ag, Au;

II group Be, Mg, Zn, Cd, Hg.

For the same reason, course of the second is non-repetitive — as well as the s-potential for the indicated series of elements of the second group (Table 1).

TABLE 1

Ionization potentials	Elements				
I_I	Li 5.37	Na 5.09	Cu 7.67	Ag 7.59	Au 9.22
I_I	Be 9.30	Mg 7.63	Zn 9.37	Cd 8.96	Hg 10.38
I_{II}	18.12	15.10	18.04	16.80	18.80
$I_I + I_{II}$	27.42	22.73	27.41	25.76	29.18

Thus, the primary ionization potentials in the main sub-group of Group III correspond to tearing off of p-electrons, and therefore, correspond to non-repetitive course to a lesser extent, despite the fact that Ga, In and Tl, as well as Zn, Cd and Hg, proceed to take on d-electrons (and in the base of Hg and Tl, f-electrons in addition).

The course of I and I_{III}, as well as the sum of the three ionization potentials, is again markedly non-repetitive because the second and third electrons split off from the s-orbit (Table 2).

TABLE 2

Ionization potentials	Elements				
	B	Al	Ga	In	Tl
I_I	7.28	5.94	5.97	5.76	6.07
I_{II}	24.99	18.85	20.39	18.76	20.4
I_{III}	37.70	28.95	30.66	27.85	29.8
$I_I + I_{II} + I_{III}$	69.97	53.74	57.02	52.37	56.27

A very similar picture is also observed in the sub-groups:

C, Si, Ge, Sn, Pb,
N, P, As, Sb, Bi,
O, S, Se, Te, Po,
F, Cl, Br, I, At.

Also, in those cases where potential is concerned, (the potentials whose number corresponds to the group number, or is one less than this group number), the s-electrons begin to participate in the orbits of chemical

compounds, these s-electrons projecting themselves under the screen made of ten d-electrons (and sometimes made with an additional 14 f-electrons), as the result of which there appears a marked non-uniformity. Potentials of lower values (p-potentials) display non-uniformity not at all, or very poorly, increases simply being displaced by sharper decreases.

Sub-groups:

K,	Rb,	Cs,	Fr,
Ca,	Sr,	Ba,	Ra,
Sc,	Y,	La,	Ac,
Ti,	Zr,	Hf,	–,
V,	Nb,	Ta,	–,
Cr,	Mo,	W,	–,
Mn,	Tc,	Re,	–,
Fe,	Ru,	Os,	–,
Co,	Rh,	Ir,	–,
Ni,	Pd,	Pt,	–.

i.e., a series of elements whose potentials correspond either to rupture of s-electrons for construction of the d-screen, or to rupture of d-electrons themselves, are not related to the marked non-uniformity discussed here. For illustration, the authors have presented Fig. 1 for summated potentials of the principal and additional sub-groups of I, II, III and IV group elements.

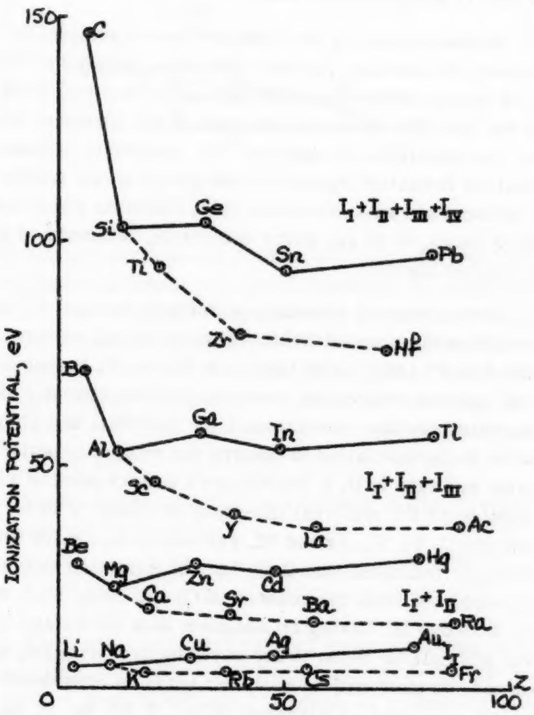

Fig. 1.

The above-discussed non-uniform, zig-zag course for individual potentials (equal in value to the number of the group of elements, or one less than the group number) can be designated secondary periodicity – in distinction to the principal periodicity which characterizes all elements series which are distributed without gaps in order of nuclear charges, secondary periodicity being evident upon examining the group lines which bind only elements of specific groups in the system.

Thus, in Fig. 2, with its characteristically classical principal periodicity, indicated by solid lines, dotted grouping lines can be seen; in this case, secondary periodic non-uniform lines for the first potential will be only lines for the series:

Li, Na, Cu, Ag, Au;
Be, Mg, Zn, Cd, Hg.

Similar graphs can be plotted for any potential, for example, in Fig. 2, the author presents a picture of the third potentials, on which the grouping lines for the sub-groups are the secondary periodics:

B, Al, Ga, In, Tl;
C, Si, Ge, Sn, Pb.

If an obligatory non-uniformity is not required for the course of the grouping lines, and alternation of steeper and more sloping sections is satisfactory, then the phenomenon can, of course, be observed in other sub-groups. In such more general form, it is better not to use the term "secondary periodicity", but simply to talk about the phenomena of d- and f-consolidations of the electronic bond (mainly of the s- and p-electrons, and to some extent of the d-electrons).

D. I. Mendeleev realized clearly that changes in properties of the elements in vertical columns of the Table can occur non-uniformly in a number of cases, thus interfering with interpolation and prediction of the properties

of undiscovered elements, as the result of which he worked out such predictions by averaging values along not only the vertical, but along the horizontal as well, i.e., by crosswise utilization of information about the properties of the four neighboring elements.

Later, Byron [2] drew particular attention to the non-uniformity of modified properties of related chemical compounds from the principal sub-groups V, VI, and VII elements of the system, and termed this phenomenon secondary periodicity. Lately the phenomenon of non-uniformity in properties of chemical compounds for some groups of the system has been of interest to a large number of investigators: Rott [3], Kapustinsky [4], Balarev [5] and Shishokin [6]; foreign scientists have forgotten the existence of Byron's classical work.

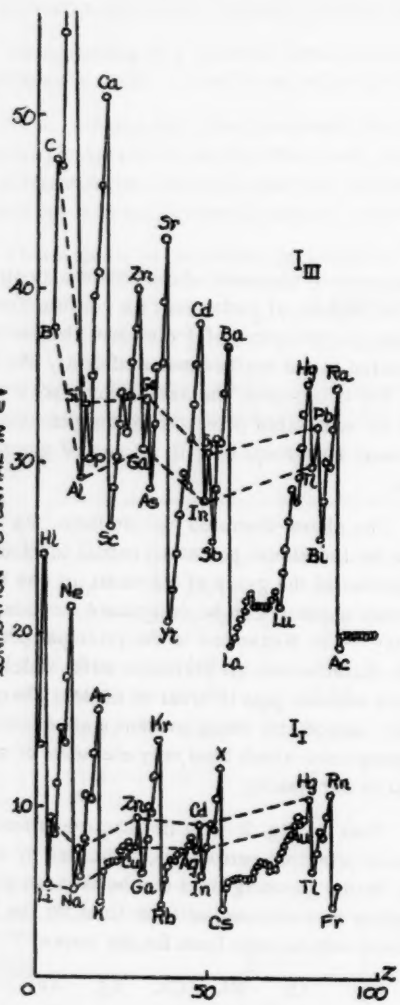

Fig. 2.

Now turning to the question of causes for the existence of a non-uniform course in properties of chemical compounds, the authors have assumed that secondary periodicity in properties of chemical compounds — which is complicated by thermodynamic and chemical interactions — can be explained as a reflection of secondary periodicity in electronic characteristics of the free electronic shells of the atom, in the general way as was presented above.

Without repeating the already-known examples in chemistry of secondary periodic exhibition in heats of formation of various oxides and chlorides, the author will point out only the fact that the cases indicated in the literature fall under the description in question, i.e., secondary periodicity in heats of formation appears in sub-groups of the system and the valences are associated with those electrons which are under a strong, or in any event noticeable, influence of d- and f-consolidations.

Byron observed secondary periodicity in heats of formation of the oxides and chlorides of the principal sub-groups of groups VII, VI and V; with respect to Group IV, he could not decide upon an evaluation, since the thermochemistry of germanium was then non-existent; by 1932 Rott had already data for GeO_2, but failed to observe the secondary periodicity, because contrary to D. I. Mendeleev's correct point of view, he considered the principal sub-group of Group IV to be the succession C, Si, Ti, Zr and Hf, and not C, Si, Ge, Sn and Pb. Rott simply indicated that GeO_2 heat of formation cannot be interpolated from the heats for SiO_2 and SnO_2. With regards to Group III, having no adequate data for Ga and In, it was difficult for Byron to say anything in this regard; Rott possessed thermochemical data, but again he considered the principal succession of elements to be: B, Al, Sc, It, La, and therefore did not notice anything, except for the heat of formation of Ga_2O_3 which could not be interpolated from the heats for Al_2O_3 and In_2O_3.

In order to enlarge information regarding secondary periodicity phenomena for the tetravalent states of the sub-group for Group IV elements, the author, along with Vasilkova, undertook a study of the heats of formation for compounds of these elements with magnesium. The investigation, which was completed in 1949, indicated [7] that these heats change non-uniformly upon transition from element to element, as was to be expected. Following this investigation, the author, together with Arya and Lakhtin [8], studied heats of formation for magnides of trivalent compounds of the principal sub-group of Group V, for which non-uniformity was again found — and this despite the fact that in such cases the valence electrons were not s, but p; d- and f-consolidations of the atoms, however, were found sufficient to be reflected in the heats of formation of the compounds. For comparison of non-uniform functions found by the authors with standard uniform course of heats of formation for magnesium compounds with elements of Groups VII, VI, V and IV, the heats of formation calculated per gram-atomic-weight of magnesium

are compared in Fig. 3. As can be seen from Fig. 3, heats of formation of silicide and phosphide, of stannide and stibnide, of plumbide and bismuthide, approximate each other in pairs. Discrepancy in the case of germanide and arsenide is perhaps connected with lower accuracy in determination, because of the small amount of germanium

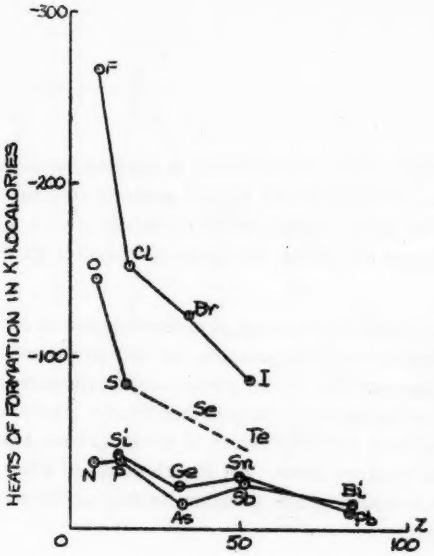

Fig. 3.

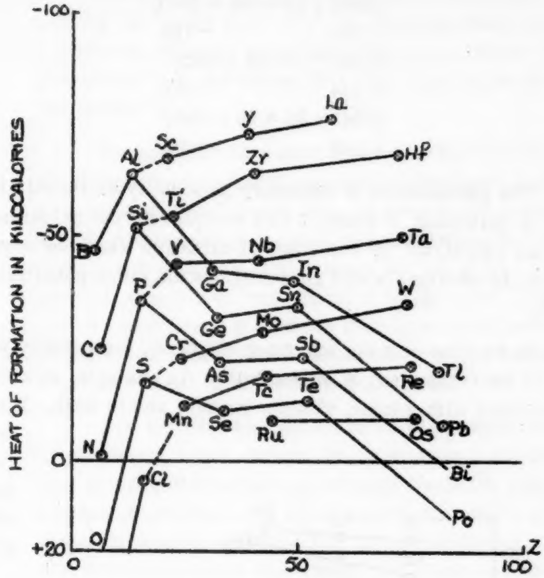

Fig. 4.

which was available to the authors, and from the indefiniteness of heat formation for arsine. To illustrate the rule of uniformity in course of heats of formation for compounds of the main sub-groups of the elements, there can be quoted a large amount of experimental material, using literature data. Thus is produced a very informative picture on the comparison of heats of formation for higher oxides of various elements. There can be seen in Fig. 4 a typical picture variance in course of the group lines for the main and the sub-groups. Since compounds corresponding in degree of oxidation to the group number display secondary periodicity with particular clarity, higher oxides were, therefore, used as much as possible for Fig. 4. Values for heats of formation were, before plotting points on the graph, standardized by recalculating to 1 gram equivalent of oxygen.

In Fig. 5 are presented (analogously to Fig. 4) heats of formation for the chlorides, claculated to 1 gram atomic weight of chlorine.

The figures presented have an important value in understanding two long-known rules concerning changes in thermal stability of higher-valence compounds for sub-groups of the system of elements in transition from top to bottom of a vertical column. Decrease in uniformity of ionization potentials for minor sub-groups, related to an increase in principal quantum numbers, results in a consolidation of higher-valency compounds when moving from top to bottom in the system. Thus, for example, WO_3 is more stable than CrO_3, WCl_6 exists, and Cr gives, with difficulty, $CrCl_4$; Re_2O_7 is more stable than Mn_2O_7, OsO_4 exists, and FeO_4 is not formed; so forth.

Secondary periodicity of ionization potentials in the main sub-groups produces a reverse situation for higher oxides of the main sub-groups; as a result, Bi_2O_5 does not form, PbO_2 is a strong oxidant similar to Tl_2O_3; HgO is less stable than ZnO, the gold oxides are less stable than the copper oxides.

For the same reason, As_2O_5, and especially SeO_3, are found to be strong oxidants, while higher oxides of fluorine and bromine are not yet known.

Difference in display of secondary periodicity by higher and lower oxides is readily seen in the case of main sub-groups elements of Group IV, which is indicated in the course of their heats of formation (Q for one gram formula weight) which is presented in Fig. 6. Because of secondary periodicity in heats of formation of higher oxides, the lower oxides, GeO and PbO are rendered stable, and are not inclined to a separation reaction to dioxide and the free element, while CO, SiO and SnO are capable of exothermal reaction (disproportionation).

In actuality: $2CO - 40 = C + CO_2$
$+54 \quad -94$
$2SiO - 8 = Si + SiO_2$
$+200 \quad -208$
$2GeO + 28 = Ge + GeO_2$
$+154 \quad -126$
$2SnO - 4 = Sn + SnO_2$
$+134 \quad -138$
$2PbO + 38 = Pb + PbO_2$
$+102 \quad -64$

The phenomenon of secondary periodicity exists only for equilibria which are produced in aqueous solutions. Thus, in particular, if standard free energies for the oxidation reaction of elements (in normal aqueous-acid solution) are calculated for that stage of oxidation which corresponds to the group number of the elements, then a picture can be obtained which characterizes the redox potentials of the main and of the sub-group elements (Figs. 7 and 8).

In the case of main sub-group elements, a secondary periodicity is plainly evident, and there becomes clear (Fig. 7) the comparison of oxidizability, for example, of nitric, phosphoric and arsenic acids, or the comparison of sulfuric acid with selenic, chloric, bromic, and so forth. It can also be seen that as the group number increases (i.e., the degree of oxidation), there is displayed a greater and greater tendency to coordination of oxygen atoms around the central oxidized atom. For the elements of other sub-groups a similar graph gives uniformity in the course of potentials.

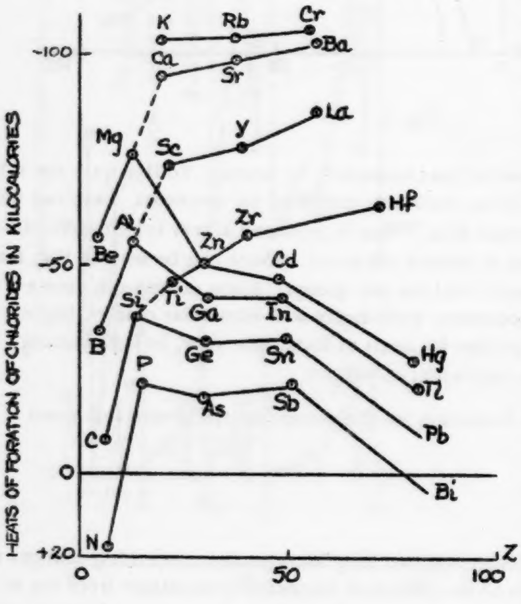

Fig. 5.

In light of the above situation, there becomes particularly evident the power of application, which was utilized by D. I. Mendeleev for prediction of the properties of gallium and germanium compounds, whose quantitative characteristics, on the basis of secondary periodicity, diverge noticeably from the average values between aluminum and indium, silicon and tin; with respect to scandium, prediction was easier since it lies in the sub-group, and the transition of Al—Sc—Y is more uniform than for the series Al—Ga—In.

In fact, the arithmetic mean of heats of formation of Al and In oxides is equal to 310 kcal, and for Ga has a heat of formation equal to 256 kcal; the average values for heats of formation of Al and Y oxides is equal to 410 kcal, and Sc also 410 kcal.

In individual cases of secondary periodicity, we can see how profound and in what detail the principal of periodicity of properties plays a role with respect to atomic electronic shells and the properties of chemical compounds. Both energy of crystalline structures and of gaseous molecules (ionic and covalent bonds), as well as energy of ion hydration (monoatomic or even polyatomic hydrolysis products, or complex formation) changes systematically on the whole with the sum of the ionization potentials, which correspond to specific degrees of oxidation. Depending upon whether the change in potential sum occurs more sharply or less so, than the change in corresponding energies for the lattice hydration energies, the heats of formation of the compounds and their heats of dissolution (in dilute solutions) change adiabatically or isothermally with the potential sums, in other words, by one way or the other, their periodicity is not only repeated in a general form, but also in more minute details. The situation is, of course, complicated with increase in the temperature, and often with ordinary temperatures in solutions, when entropy and temperature factors begin to play an important role, which are not considered from the viewpoint of periodicity in ionization potentials.

Without doubt, chemistry stands on the threshold of a course of investigation into periodicity of enthalpy, and even more so of free energies of formation for even the most simple compounds. The fact of periodicity

itself, and a display of its most important details, for example of secondary periodicity, is well-known to us at present, but the real functional relationships which should be expressed in mathematical form remain a closed chapter.

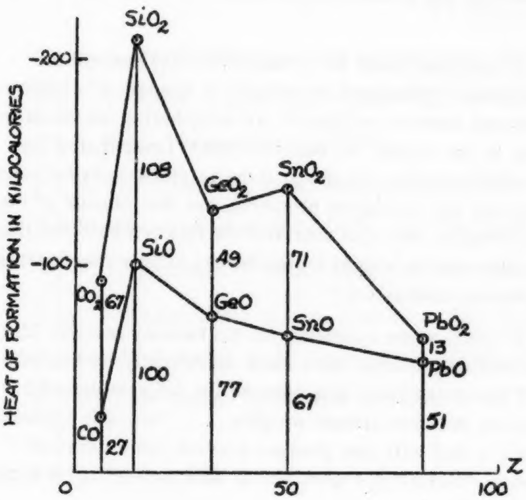

Fig. 6.

Back in 1871 [9], D. I. Mendeleev wrote concerning the known law: ". . . the function itself is not yet known, and only one of its properties is known — periodicity"; on the whole, this expression is true up to the present day.

Despite such slow development of the science in the direction of finding a quantitative mathematical expression of the Periodic Law, our esteem for it grows, and we are coming to increasingly understand that here is an outstanding law, and perhaps not just a law, but a general principle of periodicity, if by the term "principle" we understand it to mean that from which develop, as individual cases, many standard laws which can be expressed in concrete mathematical terms.

The Periodic Law should be considered the basis of chemistry, which defines the intermittent, qualitative modifications which accompany transition from one element to another, and which asserts periodicity of same, depending upon behavior of the combining nuclei and the external electrons of the atoms and qualitative changes in the series of elements arranged in order of increasing nuclear charge from hydrogen to centurium.

The D. I. Mendeleev Periodic Law is not expressed by an continuous, functional relationship; apparently, it cannot be completely characterized by any one general mathematical formula, because it is found to be a general and basic principle which possesses an infinite number of individual cases, which can, it is hoped, only be approached by experiment and mathematics.

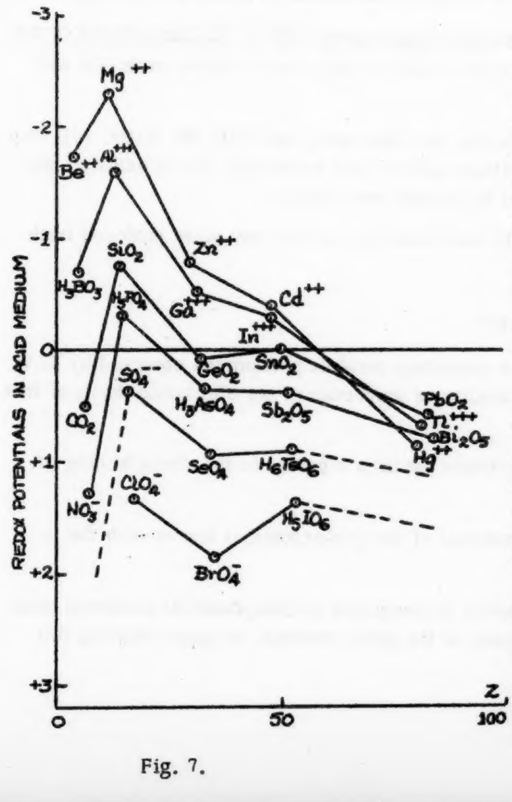

Fig. 7.

Touching only in a very general way upon the philosophical principal of transition from quantity to quality, let us apply the Periodic Law, as a scientific principle, to the specific system of qualitative characterization of the elements, i.e., let it be related to the behavior of free atoms; its individual expressions are varied and numerous, and applicable to the elements or chemical compounds each in a characteristic modified and complex form. Each specific case, therefore, should be related to periodicity of some specific physical or chemical property and its quantitative characteristics measured by experiment. Mathematical expressions of this law in such specific instances will, of course, be different.

The periodic principle laid down for electronic shells of the atom systems, intimately related to the ideas of saturation capacity of the shells and pairing of the electrons, has developed for chemistry a fundamental significance similar to the principles of quantum statistics and thermodynamic concepts of entropy and temperature for polyatomic systems, and to the principle of conservation of mass and energy for all of matter. The superposition of thermodynamic principles upon the periodic principle of D. I. Mendeleev, however, should produce true laws governing the formation, stability, and conversion of elements and chemical compounds; the author has in mind those laws which are closely associated with the ideas of saturation, coupling and substitution, to which D. I. Mendeleev gave so much attention in his chemical approach.

It is well-known that D. I. Mendeleev, in his classical formulation of the Periodic Law, compared forms of the compounds with atomic weights of the elements. In 1889, he wrote [1] thus: "To explain and to express the Periodic Law means to explain and to express the cause of the law of multiple relationships, differences in the elements, and changes in their atomic structure, and at the same time, requires an understanding of what is meant by mass and attraction." Thus, it can be clearly seen that D. I. Mendeleev actually placed before science two problems which, in modern terminology, can now be expressed as the problem of the nature of electronic shells and the nature of atomic nuclei.

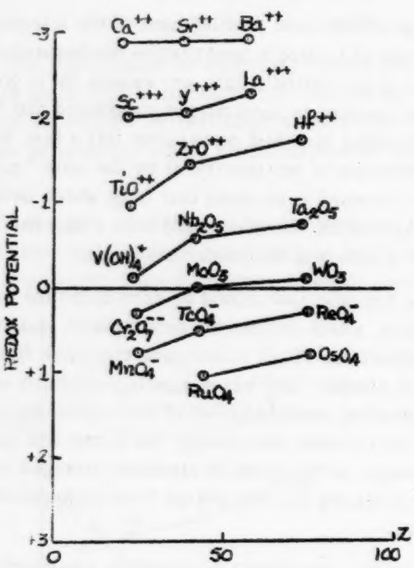

Fig. 8.

In the same year, D. I. Mendeleev [1] noticed that Ridberg (1885) "observed periodicity in changes of differences between atomic weights of two neighboring elements in relation to the atoms. A. Bazarov (1887) investigated the same subject, taking not the arithmetic differences between neighboring and analogous elements, but the relation of their atomic weights, and also observed the relation between them that as the atomic weight increases, the ratio either increases or decreases, alternately."

In 1889, when appearing for his Faraday lecture, D. I. Mendeleev commented even more specifically on this subject: "If accuracy can be improved for definite periodic differences between atomic weights . . ., then it is apparent that such a tool will also produce a much more detailed method of controlling experimental data pertaining to atomic weight values".

At the present time, the idea of nuclear periodicity is universally recognized and has been developed extensively by many authors.

In 1889, D. I. Mendeleev wrote [1]: "Periodic change in simple and complex bodies is subject to some higher law, concerning which nature and cause there are, today, no means for grasping. In all probability, it is hidden in the fundamental beginnings of internal mechanism of atoms and particles."

Taking into account the existence of independent and complex periodicities, both in the nucleus and in the electronic shells of the atom, it can be assumed that there will indeed come a day when a higher principle will be found which will embrace both periodicities.

The old, titanic ideas of a great Russian chemist live on in the new chemistry, and with the latter, will step over into future centuries, retaining not only the brilliance, communicability and creativity, but in addition, acquiring newer meanings, and unfolding in an infinite diversity of individual conclusions.

The periodicity principle discovered by D. I. Mendeleev is inexhaustible, as with any other profound truth of the material world.

SUMMARY

1. It has been demonstrated in the present article that the secondary periodic phenomena observed by E. V. Byron for properties of chemical compounds are a reflection of analogous properties of the electronic shells of free atoms of the chemical elements.

2. The cause of secondary periodicity residing in the electronic shells is inherent in the strengthening of d- and f-electron valence bonds.

3. The indicated strengthening is most evident in the properties of the s-electrons, is less so with the p-electrons, and still less for d-electrons.

4. The result of secondary periodicity appears most markedly in properties of compounds of elements composing the main sub-groups of the system, corresponding in valence to the group number, or approximating this value.

5. Specific rules for the pattern of change in thermal stability of higher-valence compounds in sub-groups of the system are dependent upon secondary periodicity.

6. Secondary periodicity appears not only for the heats of formation of chemically-pure compounds, but also for redox potentials in aqueous solutions.

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* See Consultants Bureau Translation, page 929.

COMPLEX FORMATION OF THE ANION TYPE, BETWEEN POTASSIUM AND SODIUM PYROPHOSPHATES AND OXIDE SALTS OF THE TYPE MeO_4'' (Me=S, Mo, Cr, W)

A. G. Bergman and M. L. Sholokhovich

Complex formation between salts with common anions (cation complexes), for example $KCl \cdot MgCl_2 = K[MgCl_3]$, have up to the present time received considerably more study than complexes of the anion type, formed from salts with a common cation and with different anions, for example, $AgNO_3 \cdot AgCl$, $BaF_2 \cdot BaCl_2$.

A systematic investigation of mutual systems wherein are found two different cations with the same common anion, and two others with the same common cation, has led to an accumulation of interesting material on anion complexes.

At the present time a large number of anionic complexes have been obtained, among which many are characterized by sharply marked maxima on the melting point curves, with rather high melting points, as for example, $BaF_2 \cdot BaCl_2$ 1008°; its heat of formation was 15.1 kcal [1]. It has been considered up to the present time that complex formation is much more pronounced between potassium salts and other metals with common anions than for corresponding sodium salts.

Data given in the present article from an investigation of eight binary systems, as well as collected, extensive experimental material on the chemistry of molten salts, have shown a number of cases where the sodium salt displays a greater tendency to complex formation than the corresponding potassium salts.

TABLE 1

1st column = mol % of $K_4P_2O_7$; 2nd column = temperature at which first crystals appeared (E = eutectic)

1	2	1	2	1	2	1	2
$(K_2SO_4)_2-K_4P_2O_7$		$(K_2WO_4)_2-K_4P_2O_7$		$(K_2CrO_4)_2-K_4P_2O_7$		$K_4P_2O_7-(K_2MoO_4)_2$	
0	1070	0	928	0	984	0	1095
15	1040	6	916	12	948	20	1018
25	1018	12	904	18	930	25	995
35	992	18	888	24	920	30	982
40	976	23	870	30	902	32	968
45	962	27	862	35	890	35	956
50	934	31	848	40	876	40	932
55	898	33	840	42	880	45	910
60	898	36	852	45	888	50	886
65	936	39	869	50	906	55	866
70	960	45	904	55	920	60	845
75	996	50	930	60	936	62	830
80	1018	54	946	65	952	65	824
85	1046	57	960	70	968	70	842
				75	986	75	854
				80	1006	80	870
				85	1024	85	888
				90	1045	90	898
						95	911
E at 57.5% $K_4P_2O_7$ and 882°		E at 39% $K_4P_2O_7$ and 836°		E at 40% $K_4P_2O_7$ and 876°		E at 64% $K_4P_2O_7$ and 822°	

In Tables 1 and 2, and in Figs. 1 and 2 are given results of investigation of eight binary systems, of which four were formed from potassium pyrophosphate with potassium sulfate, chromate, molybdate and wolframate (Fig. 1), and the corresponding four – from analogous sodium salts (Fig. 2). Experimental data given in the tables indicated are incomplete for the sake of brevity.

TABLE 2

1st column = mol % of $Na_4P_2O_7$; 2nd column = temperature at which first crystals appeared (E = eutectic; P = transition point)

1	2
$(Na_2CrO_4)_2-Na_4P_2O_7$	
0	816
6	787
9	777
12	765
18	806
21	838
24	853
27	875
30	903
33	916
36	914
39	912
42	912
45	903
48	886
51	875
54	866
57	853
60	847
63	866
70	916
75	934

E_1 at 12% $Na_4P_2O_7$ and 765°
E_2 at 59.5% $Na_4P_2O_7$ and 833°

1	2
$(Na_2MoO_4)_2-Na_4P_2O_7$	
0	690
3	684
6	674
9	663
11	663
13	684
15	714
17.5	732
21	756
24	774
27	786
30	796
35	810
40	818
45	819
48	819
50	820
52	816
57	826
66	865
75	906
85	946
90	966

E_1 at 10% $Na_4P_2O_7$ and 654°
E_2 at 54% $Na_4P_2O_7$ and 807°

1	2
$(Na_2WO_4)_2-Na_4P_2O_7$	
0	694
6	676
9	666
12	656
15	647
18	675
21	706
24	720
27	730
30	740
33	751
36	758
39	764
43	778
45	788
48	808
50	818
57	848
64	880
70	898
78	928
88	960

E at 15% $Na_4P_2O_7$ and 647°

P at 42% $Na_4P_2O_7$ and 767°

1	2
$Na_4P_2O_7-Na_2SO_4$	
0	999
16	946
22	926
28	898
31	880
35	866
37.5	852
40	840
43	828
49	794
52	780
55	763
58	748
61	760
64	770
67	781
70	793
73	803
76	814
79	824
82	834
86	846
88	851
91	866

E at 58% Na_2SO_4 and 748°

It follows from the data obtained that the four binary systems formed by potassium pyrophosphate represent special eutectic systems, without complex formation on the liquidus curves. Subsequent investigation by thermographic analysis of the solid state should render evident the presence or absence of chemical affinity in the solidus. For the system $Na_2SO_4-Na_4P_2O_7$, the melting curve indicated a eutectic, the solidus region should also have been in detail. With sodium chromate, molybdate and wolframate, sodium pyrophosphate formed the following compounds $Na_4P_2O_7 \cdot 4Na_2CrO_4$, melting without decomposition at 916°, $Na_4P_2O_7 \cdot 2Na_2MoO_4$, also melting without decomposition at 821° and $Na_4P_2O_7 \cdot 2Na_2WO_4$, melting without decomposition at 767°. Of the systems indicated, experimental difficulties arose only during an investigation of the system $(Na_2CrO_4)_2-Na_4P_2O_7$. In this case, the equilibrium state of the system was reached only during numerous heating and cooling processes.

In this connection, it was possible to successfully demonstrate chemical affinity in the system only by investigating the given system through the method of additives. Investigation of the system by the method of melting temperatures, determined by the first appearance of crystals, led to the same conclusion only after repeated cooling and heating of each compound.

It is interesting that for the series of systems with sodium and potassium fluorides, and with oxygen-containing sodium and potassium salts, there exists a reverse relationship in complex formation.

Potassium fluoride forms compounds (melting with decomposition) with potassium pyrophosphate, chromate [2], tetrabromate [3] and carbonate [4], whereas for the corresponding systems with sodium salts, simple eutectics are formed.

Sodium and potassium fluorides with the corresponding sulfates form compounds melting without decomposition $KF \cdot K_2SO_4$, m.p. 887° [5] and $NaF \cdot Na_2SO_4$ [5], melting at 781°. Replacing the sulfate ion by pyrophosphate,

and the fluoride ion by MeO_4'' anions of the sixth group (SO_4'', CrO_4'', MoO_4'', WO_4''), eutectic systems are obtained for the potassium series. and for the corresponding sodium salts, systems of the compounds are formed.

There is also observed complex formation in varying degree with other combinations of potassium and sodium salts. Thus, potassium nitrate and acetate form compounds melting without decomposition at 238°, whereas the corresponding sodium salts do not form such [6].

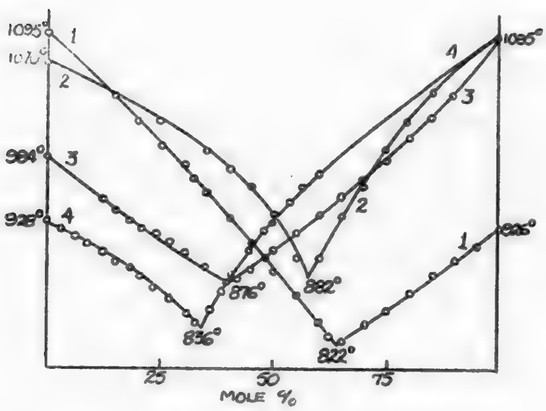

Fig. 1. Melting curves for the binary system potassium pyrophosphate. 1) otassium molybdate; 2) potassium sulfate; 3) potassium chromate; 4) potassium wolframate.

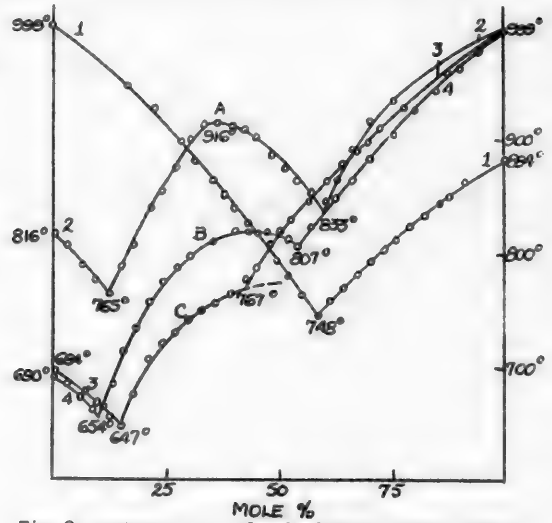

Fig. 2. Melting curves for the binary system sodium pyrophosphate —: 1) sodium sulfate; 2) sodium chromate; 3) sodium wolframate; 4) sodium molybdate.

A) $Na_4P_2O_7 \cdot 4Na_2Cr_2O_4$; B) $Na_4P_2O_7 \cdot 2Na_2MoO_4$; C) $Na_4P_2O_7 \cdot 2Na_2WO_4$.

On the other hand. sodium hydroxide and sodium nitrate form two compounds of the composition 2:1 and 1:1, melting without decomposition at 272° and at 271.5° [7], whereas KOH and KNO_3 give one compound of the composition 1:1, melting without decomposition, at 236.5°; note that KOH and KNO_3 have higher melting points (406 and 337°) than NaOH and $NaNO_3$ (320 and 308°). The same phenomenon is observed to a somewhat lesser extent for the alkali-nitrite systems. The compound $NaOH \cdot NaNO_2$ melts without decomposition at 206° [7] and $KOH \cdot KNO_2$ at 170° [7]; potassium nitrite melts at 436°, and $NaNO_2$ at 282°. This phenomenon is even more sharply evident between caustic alkalies and sodium potassium chromates: KOH and K_2CrO_4 form a eutectic system, and NaOH and Na_2CrO_4 form two compounds melting with decomposition [8].

The examples which have been quoted are already sufficient to demonstrate that the tendency to complex formation is not an innate property of any element by itself, but depends upon mutual relations between two salts (upon ionic radii and their general moments, upon external electronic shells, reciprocal polarization, and also upon that correlation which appears in formation of a crystalline lattice).

Moreover, the examples quoted confirm the status of chemistry of the molten salts which was established long ago, namely that the chemical properties of potassium and sodium differ considerably, and if there is a compound with similar type of sodium and potassium salts, that such is a coincidence rather than the rule. There are known a number of compounds characteristic only for sodium salts, or for potassium salts. Thus, for example, potassium salts form characteristic langbeinite complex $K_2SO_4 \cdot 2MgSO_4$ [9] (where instead of Mg, there can be Zn, Ni, Co, Mn, Pb), whereas sodium salts form the compound $3Na_2SO_4 \cdot MgSO_4$ and of composition $Na_2SO_4 \cdot 3MeSO_4$ [10]. These types of compounds are completely absent in potassium salts. Compounds of the composition 1:1 are also formed with sodium and potassium, but in aqueous solutions they produce a different series of the schoenite type $K_2SO_4 \cdot MeSO_4 \cdot 6H_2O$ (Me = Zn, Fe, Ni, Co), whereas sodium sulfate gives the astrakanite type $Na_2SO_4 \cdot MeSO_4 \cdot 4H_2O$. Further, we have the characteristic $KCl \cdot MgSO_4$, for the kainite type salt, where potassium can be replaced by Rb, Cs, Te, NH_4; Mg by Zn; Cl' by Br', and I' [11]. Sodium salts do not form complexes of the kainite type.

SUMMARY

1. By visual polythermic method, the following binary systems have been investigated: 1) $(Na_2SO_4)_2 - Na_4P_2O_7$; 2) $(Na_2CrO_4)_2 - Na_4P_2O_7$; 3) $(Na_2MoO_4)_2 - Na_4P_2O_7$; 4) $(Na_2WO_4)_2 - Na_4P_2O_7$; 5) $(K_2SO_4)_2 - Na_4P_2O_7$; 6) $(K_2CrO_4)_2 - K_4P_2O_7$; 7) $(K_2MoO_4)_2 - K_4P_2O_7$; 8) $(K_2WO_4)_2 - K_4P_2O_7$.

2. It has been established that for all systems where potassium salts participate, there is no complex formation.

3. In binary systems 1, 2 and 3, where sodium salts participate, compounds are formed, in contrast to similar systems where potassium salts participate.

4. The results obtained attest to profound differences in the chemical properties of sodium and potassium salts.

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COMPLEX FORMATION REACTION BETWEEN DIVALENT COBALT AND DIMETHYLGLYOXIME

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Dimethylglyoxime, by reacting with salts of divalent cobalt in neutral or alkaline medium, forms a soluble compound of yellow-brown color. This reaction, along with many other reactions of α-dioximes with metals, was discovered by Chugaev at the turn of the 20th century [1]. It is known, however, that Chugaev did not succeed in isolating either the dioximine of simple form $Co(HDm)_2$ (HDm^-, monovalent dimethylglyoxime anion), or any other compound of determined composition with divalent cobalt, despite evidence of its formation in aqueous solution. Attempts of other investigators who worked in this field after Chugaev were also fruitless. In 1923, Feigl and Rubenstein [2], and later Peshkova [3] isolated a green compound of the composition $Co(H_2Dm)_2Cl_2$, by heating acetone (or alcoholic) solution of cobalt chloride with dimethylglyoxime, which for a long time was considered to be the divalent cobalt compound. Upon dissolving in water, this compound forms the same yellow-brown colored solution as when the cobalt salt is mixed with dimethylglyoxime under the usual conditions. Proceeding from this fact, Feigl assumed that at the base of soluble dioximines of cobalt oxide there lies the compound $Co(H_2Dm)_2X_2$, where X^- equals a monovalent acid radical, and H_2Dm equals the dimethylglyoxime molecule.

Quite a number of works have been dedicated to a study of the properties of the compound $Co(H_2Dm)_2Cl_2$. However, data referring to the properties of this compound, including the valencies of cobalt in it, have been contradictory, and deductions about the structure do not agree with classical concepts of Chugaev regarding the dioximine structure. On the other hand, there is no data in the literature concerning the complex formation reaction between divalent cobalt and dimethylglyoxime under the usual analytical conditions. Instances are known, however, where reaction with α-dioximes proceeds differently, depending upon the medium. Thus, for example, in anhydrous solvents (alcohol, acetone) copper forms with dimethylglyoxime an addition product of the composition $Cu(H_2Dm)Cl_2$ [4], and in aqueous solution, $Cu(HDm)_2$ [1].

In the present work, the authors have given results of an experimental study of the reaction between divalent cobalt and dimethylglyoxime.

EXPERIMENTAL

Synthesis and Analysis of the Compound $Co(H_2Dm)_2Cl_2$

The compound $Co(H_2Dm)_2Cl_2$ was prepared according to the method of Feigl by heating an acetone solution of cobalt chloride and dimethylglyoxime mixture taken in the mole ratio of 1:2 under reflux, for the purpose of studying its properties. It was found that the yield of crystal product was higher if the reaction mixture was not heated, but allowed to stand at ordinary temperature in an oven for 24 hours. The resulting compound was readily soluble in water, but upon acidification of the aqueous solution, again separated in the form of large, lustrous, dark-green crystals. This property was utilized for recrystallization. A saturated aqueous solution of the crude product was acidified with concentrated hydrochloric acid until the crystals had precipitated, which were then immediately filtered off, washed first several times with small portions of cold water, and then with acetone. After drying at 105°, the percentage composition of cobalt and of chlorine was determined. Cobalt was determined by gravimetric means as the hydrochloride after acidification of the organic residue from nitric acid and subsequent vaporization with sulfuric acid. For determination of chlorine, the batch was dissolved in water and the resulting solution heated almost to boiling, keeping in the heated stage for 30 minutes. After addition of silver nitrate, the mixture was cooled to 30-40°, and 20 ml of nitric acid, 1:10, then added. The mixture was stirred without heating to the complete coagulation of silver chloride. The procedure was then carried out as usual.

16.20% of cobalt was found and 18.95% of chlorine. Calculation carried out on the basis of analytical data (content of dimethylglyoxime by difference) gave for the components a ratio of $Co : H_2Dm : Cl = 1:2:2$, which corresponds to the data of Feigl, as well as that of Peshkova.

Properties of the Compound Synthesized from Acetone Solution

Feigl considers that for the given compound cobalt is divalent. His conclusionis based on the assumption that he obtained an identical compound in the presence of hydroxylamine as a reducing agent. In his opinion, the compound $Co(H_2Dm)_2Cl_2$ is an addition product, i.e., the acid radicals are ionically bound (reaction with silver nitrate), and two unchanged dimethylglyoxime molecules enter into the composition of the complex ion: $[Co(H_2Dm)_2]Cl_2$ groups, instead of the grouping adopted by Chugaev. The compound hydrolyzes in aqueous solution in accordance with the following scheme:

$$[Co(H_2Dm)_2]Cl_2 + H_2O = [Co(H_2Dm)_2](OH)Cl + HCl, \qquad (1)$$

which Feigl verifies only from analytical data for the hydrolysis product which precipitates when a saturated aqueous solution of $Co(H_2Dm)_2Cl_2$ is allowed to stand. Feigl does not furnish any other information concerning the properties of the green compound and its hydrolysis product. Feigl also refers $Co(H_2Dm)_2Br_2$ and $Co(H_2Dm)_2I_2$, to the same type of compound which he obtained according to the above-indicated method. Thiele and Heilborn [5] also limited themselves to a study of the individual properties of the green compound. They observed that when treating it with sulfuric acid, there was no evolution of hydrogen chloride, which should have taken place if chloride ions were present in the external medium. Proceeding from this fact, they proposed a structure with chlorine bound non-ionically: $[Co(H_2Dm)_2Cl_2]$. Heiber and Leutert [6] came to the same conclusion about the structure on the basis of a small electroconductivity value for the acetone solution. Indications are found in later works that the compound $Co(H_2Dm)_2Cl_2$, and its hydrolysis product, are similar to other complex compounds of trivalent cobalt, in that they are diamagnetic, and hence that trivalent cobalt, and not divalent, enters into the composition. In accordance with this deduction, it was found that a property of this green compound was release of iodine from an acidified solution of potassium iodide. Sen and Ray proposed an unlikely formula with asymmetric structure for the molecule $\left[Co^{III}\begin{matrix}HDm\\H_2Dm\end{matrix}Cl_2\right]$ [7].

Taking into account the possibility of divalent cobalt oxidizing to trivalent by oxygen of the air, during synthesis of the green compound, the authors carried out a control experiment in a sealed tube, the space over the reaction mixture having been filled with carbon dioxide. It was found that in the absence of air, reaction did not proceed, heated or not, even after several days. Only upon opening the tube did green crystals of the compound immediately begin to precipitate. This fact indicated that for the given case, a trivalent compound of cobalt was formed. The correctness of this deduction is confirmed by all of the peroperties exhibited by this compound in aqueous solution, wherein it displays close analogy with the properties for dioximine complexes of trivalent cobalt [8], rhodium [9] and iridium [10] which have already been extensively studied.

The green compound dissolves in water, alcohol, acetone, but is insoluble in ether. The solubility in water at 20° was equal to 2 g/100 ml; upon addition of alkali, it was noticeably increased.

An aqueous solution of the green compound has a strong acid reaction. Upon introducing hydrochloric, sulfuric or nitric acid, the initial substance results immediately. This phenomenon can be explained either by reversibility of the hydrolytic rupture of the complex, with isolation of the acid (equation 1), or by a decrease in solubility produced by introduction of common H^+ ions, if the dissolved substance is, itself, an acid.

On the strength of the above-indicated and other properties, similar to properties for the complex dioximine acids of trivalent metals which have already been described in the literature, the following formula might be proposed for the investigated compound: $H[Co(HDm)_2Cl_2]$. Confirmation of the accuracy of this deduction depends upon determination of the sign of the colored complex ion charge, a study of the reaction with silver nitrate, measurement of electroconductivity and pH, as well as conductometric titration of the solution with alkali.

To determine the charge of the complex particle, a solution of the investigated compound, with a small amount of added potassium chloride, was placed in the lower part of a U-shaped tube containing stopcocks. The space over the stopcocks was filled with potassium chloride solution of the same concentration as was taken for the lower solution. Under the effect of current, the limit of the colored layer was displaced toward the anode; according to the structure proposed by Feigl, a complex cation should have been formed. The reaction with silver nitrate is also very characteristic. Upon addition of silver nitrate to a freshly-prepared solution of the green compound, there immediately precipitated out a silver compound with the complex ion, in the form of a crystalline yellow precipitate, and not silver chloride, as indicated in the literature. The salt was poorly soluble in water, unstable, and upon heating decomposed rapidly, splitting out silver chloride. If the solution was first heated, and then silver nitrate added, chloride ions then precipitated out immediately (see above the method for determination of chlorine in this compound). The given experiments demonstrate the presence of a complex anion in the compound, into the composition of which chlorine atoms also enter. The latter are held very loosely in the internal sphere and under favorable conditions can be displaced by solvent molecules.

To determine the basicity of the acid, the pH for a series of freshly-prepared solutions (Table 1) was measured.

TABLE 1

pH of the Solution $H[Co(HDm)_2Cl_2]$

Solution No.	Concentration		pH	
	g/100 ml	mole /l.	measured	calculated
1	0.3661	$1 \cdot 10^{-2}$	1.95	2.0
2	0.1830	$5 \cdot 10^{-3}$	2.24	2.3
3	0.0366	$1 \cdot 10^{-3}$	2.84	3.0

Upon comparing the data of Table 1 it can be seen that the measured pH values are close to theory, calculating on the assumption that the compound studied is a strong monobasic acid. Monobasicity of the acid is confirmed also by measurement of the molar electroconductivity (μ = 280 ohm^{-1} cm^2 at V = 1000 and t = 22°) and by conductometric titration. There is shown in the figure a titration curve for 0.3661 g (0.001 mole) $H[Co(HDm)_2Cl_2]$ with 0.1 N alkali solution (ordinate axis equals resistance, abscissa axis equals milliliters of alkali added).

10 ml of alkali was used for titration.

The results given above give grounds for suggesting that in acetone solution $CoCl_2$ and dimethylglyoxime, in the presence of oxygen of the air, react according to the equation:

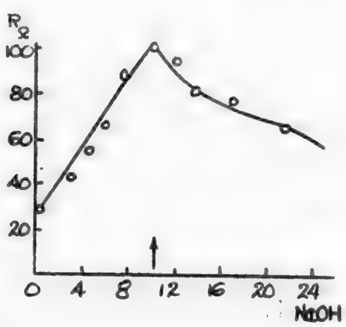
$$2CoCl_2 + 4H_2Dm + \tfrac{1}{2}O_2 = 2H[Co(HDm)_2Cl_2] + H_2O. \quad (2)$$

The compound $H[Co(HDm)_2Cl_2]$ is thus found to be an analog of the dioximine acids of trivalent cobalt, rhodium and iridium ions.

The complex acid $H[Co(HDm)_2Cl_2]$ in aqueous solution gradually reacts with the solvent, from which results a readily-crystallizing brown substance. Analytical results for it indicated the composition $[Co(HDm)_2ClH_2O]$. The substances contained, in percent: 17.30 cobalt, 10.11 chlorine. Theoretically calculated (in %): 17.15 cobalt, 10.31 chlorine.

The hydration process is reversible:

$$H[Co(HDm)_2Cl_2] + H_2O \rightleftharpoons [Co(HDm)_2Cl \cdot H_2O] + HCl. \quad (3)$$



Curve for conductometric titration of $H[Co(HDm)_2Cl_2]$ with alkali.

Introduction of acids displaces the equilibrium from right to left.

The compound $[Co(HDm)_2Cl \cdot H_2O]$ is hardly soluble in water; at 22° the solubility amounted to 0.17 g in 100 ml; negligible solubility in acetone, and almost insoluble in ether. Its freshly-prepared aqueous solution had a very low electroconductivity: μ = 3 ohm^{-1} cm^2 at V = = 1000 and t = 22°, which coincided with electroconductivity for the complex $[Co(HDm_2)NO_2H_2O]$, described in the works of Chugaev [8]. Electroconductivity increased with time. This was apparently related to "washing out" of the second coordinated chlorine ion from the internal sphere.

Apparently, the bromo- and iodo-derivatives $H[Co(HDm)_2Br_2]$, $H[Co(HDm)_2I_2]$ should also be related to the dioximine complex acids of trivalent cobalt, taken erroneously to be compounds of divalent cobalt by Feigl and others [2], as well as the compound which was isolated by Cambi from water-alcohol mixture of monomethylglyoxime with $CoBr_2$ in the presence of HBr [11].

Study of the Reaction Between the Divalent Cobalt Ion and Dimethylglyoxime in Aqueous Solution

The reaction between divalent cobalt and dimethylglyoxime in aqueous solution proceeds externally, in a manner analogous to cobalt in the nitroso-R-salt reaction. In acid medium the Co^{++} ions do not react with dimethylglyoxime. In weak acid medium, a yellow coloration appears which increases with increase of pH. If the initially alkaline solution is acidified, then the yellow color remains without apparent change. Irreversibility of the reaction makes it impossible to apply the method of physico-chemical analysis to a solution of this system.

With a mixture of Co^{++} and H_2Dm, with small excess of cobalt ions, nickel ions do not form the nickel dimethylglyoximine precipitate; consequently, dimethylglyoxime is retained by the cobalt ions more securely than by the nickel ions. The ratio of reacting components (Co^{++} and H_2Dm) in solution was determined as follows. A titrated alcoholic solution of dimethylglyoxime was added from a buret to a known amount of cobalt salt in

weak acid solution (mixture of sodium acetate and acetic acid). A drop of the solution under investigation was periodically transferred to a strip of filter paper saturated with nickel salt. The amount of reagent used for complete binding of cobalt by the complex was determined by the formation of a red spot on the indicator paper. The results are given in Table 2.

TABLE 2

Ratio of Cobalt and Dimethylglyoxime Reacting in Aqueous Solution

0.1 M $CoCl_2$ solution taken (ml)	Medium	0.1 M H_2Dm used (ml)
4.0	Weak acid	8.2
5.0	Weak acid	10.1
6.7	Weak acid	13.5
4.0	Ammoniacal	8.3
6.0	Ammoniacal	12.3
8.0	Ammoniacal	16.2

It can be seen from Table 2 that in weak acid and ammoniacal solutions, cobalt reacts with dimethylglyoxime in the ratio of 1:2.

Isolation of Co^{II}-dimethylglyoximine and Its Analysis

Chugaev hypothesized formation of $Co(HDm)_2$ in aqueous solution. Even upon combining concentrated solutions of the cobalt salt with dimethylglyoxime (alcoholic or alkaline) the compound did not separate out. Further concentration of the solution did not lead to separation of a homogeneous reaction product, evidently due to formation of a mixture of compounds of di- and trivalent cobalt. For separation of the compound, the authors set up an experiment on the basis of some general properties of dioximines. Disodium dimethylglyoxime salt solution was added in the molar ratio of 1:2 to a cobalt salt solution. The resulting mixture was treated with dilute acid. As the alkali was neutralized, a finely-crystalline yellow substance separated from solution, which was filtered off, washed with water, and dried in air. To study the properties, three preparations were made simultaneously, and the initial compound cobalt chloride, hydrochloride and nitrate were taken. Cl^-, $SO_4^{=}$ and NO_3^- ions were not found, in contrast to the above-described complex of trivalent cobalt. Upon holding the air-dried preparations in a drying compartment at 105°, the latter turned dark rapidly, and its decrease in weight was due to water loss. The percentage content of cobalt by gravimetric procedure was also determined in the form of $CoSO_4$ and nitrogen according to Kjeldahl,* as well as the water content.

Analytical results are given in Table 3.

TABLE 3

Analytical Results for Air-Dried Co^{II}-Dimethylglyoximine

Component determined	Determined in the preparation (%) from the chloride	from the hydrochloride	from the nitrate	Average	Calculated for $Co(HDm)_2 \cdot 8H_2O$
Water	34.20	34.24	34.05	34.10	33.27
Cobalt	14.26	14.05	13.92	14.07	13.62
Nitrogen	11.90	11.73	12.01	11.94	12.93

On the basis of the data given in Table 3, it can be considered that the composition of the isolated compound corresponds to the formula $Co(HDm)_2 \cdot 8H_2O$. The authors also determined the composition of this compound after drying it to constant weight at 105°. As can be seen from the data of Table 4, the analytical results confirm conclusions concerning the ratio $Co : H_2Dm$ of the complex.

TABLE 4

Analytical Results for Co^{II}-Dimethylglyoximine, Dried to Constant Weight at 105°

Component determined	Determined in the preparation (%) from the chloride	from the hydrochloride	from the nitrate	Average	Calculated for $Co(HDm)_2$
Cobalt	20.12	20.49	20.43	20.34	20.38
Nitrogen	18.15	18.21	18.15	18.18	19.38

The preparation $Co(HDm)_2 \cdot 8H_2O$ at normal temperature was difficult to dissolve in water. Only upon prolonged contact with water (over 24 hours) did it gradually begin to dissolve, but failed to reach constant solubility. Upon heating, its solubility first increased; however, after cooling the solution, no solid phase appeared. Upon further cooling and boiling, the solution changed from its yellow color to red-brown and became turbid. Because of the extremely slow attainment of equilibrium, no accurate data on solubility were obtained. $Co(HDm)_2 \cdot 8H_2O$ dissolved in butyl,

* A certain inaccuracy in this method as applied to dioximines should be mentioned; the error in determining nitrogen is equal to about 1%. The authors have obtained the same error when determining nitrogen in nickel dimethylglyoxime, the composition of which was accurately determined.

isobutyl, isoamyl alcohols and in pyridine; insoluble in alcohol, acetone, ether, toluene and xylene.

As with palladium, platinum and copper dimethylglyoximines, containing water, Co^{II}-dimethylglyoximine (anhydrous) was readily soluble in alkali hydroxide, ammonia, sodium carbonate, sodium acetate. Upon neutralization of the alkaline solutions, crystal hydrates separated in both cases. From its cobalt content in the filtrate after 10 minutes saturation, the authors determined the solubility of $Co(HDm)_2 \cdot 8H_2O$ in alkali solutions of three concentrations (Table 5).

TABLE 5

Solubility of $Co(HDm)_2 \cdot 8H_2O$ in the Presence of NaOH

NaOH concentration (in moles/liter)	Solubility (in moles/liter)
$1 \cdot 10^{-1}$	$1.3 \cdot 10^{-1}$
$1 \cdot 10^{-2}$	$1.5 \cdot 10^{-2}$
$1 \cdot 10^{-3}$	$1.6 \cdot 10^{-3}$

Solubility increased in proportion to the concentration of alkali, and was considerably higher than for the trivalent cobalt compound described above.

The solubility of dioximines in alkalies is evidently tied up with the presence in their molecules of two hydrogen atoms which have remained on the oxime groups. It is known [12] that dimethylglyoxime, when reacted with alkali, behaves as a dibasic acid, although a very weak one:

$$K_1 = \frac{[H^+][HDm^-]}{[H_2Dm]} = 8 \cdot 10^{-12} \text{ and } K_2 = \frac{[H^+][Dm^{--}]}{[HDm^-]} \approx 10^{-14}.$$

The dimethylglyoxime complexes with ions of divalent metals: Ni^{++}, Cu^{++}, Pd^{++}, Pt^{++}, Pt^{++}, $[Me^{II}(HDm)_2]$, are acid salts. On addition of alkali, the second hydrogen ion is apparently replaced by the alkali metal, with formation of an intermediate salt.

$$Co(HDm)_2 + 2OH^- = Co(Dm)_2^{--} + 2H_2O. \quad (4)$$

Formation of the complex anion in alkali solution was verified by electrolysis in a U-shaped tube, into the bottom part of which was poured the alkaline solution of Co^{II}-dimethylglyoximine in the presence of hydroxylamine. The side liquid was alkaline solution and hydroxylamine of the same concentrations. Upon electrolysis, the colored layer shifted toward the anode.

Co^{II}-Dimethylglyoximine (both aqueous and anhydrous), in distinction to nickel- and copper-dimethylglyoximines, dissolves in hydrochloric, sulfuric and nitric acids without decomposition (if the solution is not heated), forming yellow solutions. It can be isolated again from acid solution by careful neutralization of the acid with alkali.

The increased solubility in the presence of acid for this compound differs sharply from the trivalent cobalt complex described above. The solubility of Co^{II}-dimethylglyoximine increases greatly in concentrated HCl, and a green colored solution is formed, which is noticeably distinct from the color of the salts of divalent cobalt in concentrated HCl. When diluted with water, the yellow color returns. With short heating in air of the saturated complex solution in concentrated HCl green crystals separated. Analysis of this product, and qualitative analysis, indicated that in this case, the trivalent cobalt compound described above was formed.

SUMMARY

1. The properties of a dimethylglyoxime cobalt compound separating from acetone solution, which has been described in the literature, has been studied. It has been demonstrated that this compound, erroneously considered by a number of authors to be the divalent cobalt compound, has been found to be the trivalent cobalt compound. Based upon a study of the formation and properties of the compound in aqueous solution (pH, electroconductivity, charge on the colored complex ion, reaction with silver nitrate and others) it has been deduced that its structure is $H[Co(HDm)_2Cl_2]$. It has been demonstrated that the compound $H[Co(HDm)_2Cl_2]$ reacts in aqueous solution with the solvent to form the complex non-electrolyte $[Co(HDm)_2Cl \cdot H_2O]$.

2. The complex formation reaction between Co^{++} and H_2Dm in aqueous solution has been studied. In acetic and ammoniacal media, the components react in the ratio of 1:2. The complex formed is more stable than nickel dimethylglyoximine. By the method of neutralizing a mixture of solutions of the divalent cobalt salt and the disodium salt of dimethylglyoximine with acid, the compound $Co(HDm)_2 \cdot 8H_2O$ has been isolated and a number of its properties studied.

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THE PROBLEM OFCAUSES FOR INHIBITION OF SYNTHESIS OF ALDEHYDES AND CARBOXYLIC ACIDS BY THE CATALYTIC OXIDATION OF UNSATURATED HYDROCARBONS

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A number of investigations [1, 2] have been published in the literature, wherein attempts have been made to synthesize valuable organic compounds by the oxidation of aliphatic hydrocarbons with catalysts, and in particular, the synthesis of aldehydes and carboxylic acids by oxidation of individual unsaturated hydrocarbons (ethylene and propylene), as well as their mixtures in gases from petroleum cracking. In all of the works, yields of the aldehydes and acids were very small.

The purpose of the present work is a clarification of the origin and behavior of the intermediate products which appear in the oxidation process, using as an illustration the example of propylene oxidation by oxygen of the air. The authors used silver and vanadium catalyst, which is normally used for "soft" oxidation of hydrocarbons.

Oxidation was carried out by the usual flow-type arrangement. The reaction products were analyzed for total content of carboxylic acids by titration with 0.1 N KOH solution, and for total content of aldehydes, by the hydroxylamine procedure. Propylene, carbon dioxide, carbon monoxide and oxygen contents were determined by volumetric procedure using an apparatus of the Orsat type. The contact time was determined by the ratio of gas volume passed through to volume taken up by the catalyst.

In oxidation of propylene with the above-indicated catalysts, it can be presumed that aldehydes and carboxylic acids with 1 to 3 carbon atoms are formed as intermediate products.

TABLE 1

Homogeneous Oxidation of Propylene, Acetaldehyde and Acetic Acid

Experimental conditions		Composition of the initial mixture (in vol. %)				Composition of the reaction products (in vol. %)			Percentage conversion
temperature	contact time (secs)	C_3H_6	CH_3COH	CH_3COOH	O_2	initial organic compound	CO_2	aldehyde calculated for HCOH	
370°	5	2.4	–	–	20.0	2.0	0.8	0.05	16
278	3	2.4	–	–	20.0	2.1	0.6	0.14	12
400	1.4	3.0	–	–	20.0	2.9	0.2	Traces	Small
400	5	–	5.8	–	20.0	3.36	5.0	–	43
400	5	–	5.4	–	20.0	2.40	6.0	–	55
390	5	–	–	1.2	20.0	0.32	1.7	–	73
395	5	–	–	0.77	20.0	0.15	1.2	–	80
405	5	–	–	0.75	20.0	0.04	1.4	–	94

First of all, the possible role of homogeneous oxidation and thermal decomposition of not only propylene but also its possible products of incomplete combustion, should be evaluated; for the latter, acetaldehyde and acetic acid were used for the experiments. Experimental results of the oxidation are given in Table 1, from which data it can be seen that under the same conditions, propylene oxidizes homogeneously, and to a lesser extent, than does acetaldehyde or acetic acid.

It has been established in separate experiments that the substances indicated in Table 1 remain unchanged upon passage through, in admixture with nitrogen, at 400°. Thus, the complications associated with thermal decomposition are not be be feared; on the other hand, homogeneous oxidation can be a real complicating circumstance in a study of the catalytic oxidation of propylene with vanadium catalyst, which works in the range of relative high temperatures (400°).

Catalytic oxidation of propylene was first sudied with silver catalyst, with which the process became noticeable below 200°. Propylene was obtained by dehydration of isopropyl alcohol, which was exhaustively distilled on a fractionating column with efficiency corresponding to 40 theoretical plates. In these experiments temperature was varied from 200 to 250°, and the contact time from 4 to 45 seconds, and the oxygen content from 6.6 to 20%. The results obtained are given in Table 2.

TABLE 2

Propylene Oxidation on Silver

Experimental conditions		Composition of the initial mixture (vol. %)		Composition of the reaction products (in vol. %)					Percentage of conversion
temperature	contact time (secs.)	C_3H_6	O_2	aldehydes (qualitatively)	carboxylic acids (qualitatively)	propylene oxide (qualitatively)	C_3H_6	CO_2	
200°	10	1.6	20.0				1.4	0.6	12.5
230	13	2.4	20.0				0	7.4	100
230	7	2.4	20.0	None	None	Found	0	7.0	100
240	12	2.2	20.0				0	7.0	100
240	4	2.0	20.0				0.2	5.2	90
210	45	3.4	6.6	None	None	None	–	–	10
250	45	3.4	6.6				–	–	30

It follows from these experiments that upon oxidizing propylene on silver, there are found no aldehydes or acids at all, traces of propylene oxide, and a large amount of products of complete oxidation (CO_2). All three atoms of carbon are oxidized to carbon dioxide, i.e., a complete extensive oxidation of propylene occurs. To clarify the behavior of aldehyde on silver catalyst, an experiment was set up with formaldehyde, the latter being at 260° and for a contact time of 10 seconds, being passed over catalyst in mixture with air; in this case, no aldehyde was found in the reaction products, not even qualitatively, i.e., under such conditions, oxidation is complete.

Thus, in contrast with ethylene which oxidizes "softly" to ethylene oxide on silver catalyst, propylene oxidizes more extensively under the same conditions, and the process fails to stop at the intermediate phase by modification of experimental conditions.

TABLE 3

Propylene Oxidation on Vanadium Catalyst (V_2O_5) at 400°

Experimental conditions		Initial mixture (in vol. %)		Reaction products (in vol. %)						Yield of products (mol%)*				% conversion of C_3H_6	Time of catalyst work (hrs)
rate (liters per hour)	contact time (sec.)	C_3H_6	O_2	aldehydes	acids	CO_2	CO	C_3H_6	O_2	aldehydes	acids	CO_2	CO		
26	1.3	3.0	4.8	0.08	0.02	0.4	0.2	2.7	0.6	8.8	2.2	44.4	22.2	10	0.5
29	1.2	3.0	5.2	0.12	0.01	1.8	1.4	1.8	0.2	3.3	0.3	50.0	38.8	40	1.0
29	1.2	2.4	4.8	0.10	0.01	1.9	1.2	1.0	0.2	2.4	0.24	45.2	28.5	58	1.5
29	1.2	2.4	4.8	0.13	0.01	1.9	1.2	1.0	0.2	3.1	0.24	45.2	28.5	58	2.0
29	1.2	2.4	4.8	0.12	0.01	1.9	1.7	1.0	0	2.9	0.24	45.2	40.5	58	2.5
25	1.2	3.2	5.0	0.19	0.01	2.0	1.6	2.2	0.2	6.3	0.33	66.6	53.3	31	3.0
29	1.2	3.2	5.0	0.18	0.01	2.0	1.6	2.0	0.2	5.0	0.25	55.5	44.4	37	3.5
24	1.4	3.6	4.8	0.18	0.01	1.5	2.0	2.4	0	5.0	0.25	41.7	55.5	33	5.0

Oxidation of propylene was also studied by the authors over vanadium pentoxide. Small amounts of aldehydes and carboxylic acids were found among the reaction products, along with large amounts of carbon dioxide and carbon monoxide; experimental conditions were modified to increase yields of the aldehydes and carboxylic acids. It was established that optimal conditions are: a temperature of 400°, a contact time of about 1 second and an oxygen content below the stoichiometric. A series of experiments carried out under optimal conditions are shown in Table 3.

* With respect to theoretical yield, calculated on the basis of propylene converted. Sum of reaction products is not equal to 100% because of inaccuracy of the gas analysis.

As can be seem from the data of Table 3, activity of fresh catalyst is low. During the first hour and a half, it increases, and then remains constant, decreasing slowly afterward. From the products of propylene oxidation, only traces of aldehydes (0.1-0.2 vol. %) are found, even under optimal conditions, and likewise for acids (0.01-0.02%), with large amounts of CO_2 (2%) and CO (1.2-2%). This corresponds to a ratio of useful to useless products of 1:6 with fresh catalyst, and after one hour of work, to an average of 1:19.

It was not possible to increase the yield of useful compounds by modification of experimental conditions. A comparison of these data with the data of Table 1 indicates that this result cannot be limited by homogeneous oxidation, or by thermal decomposition of the reaction products.

In order to ascertain whether or not the low yields of aldehydes and of acids are the result of low formation rates for these substances, or their rapid oxidation on the catalyst, experiments were set up with formaldehyde, acetaldehyde and acetic acid.

Experiments with formaldehyde, using various mixture compositions, are given in Table 4.

TABLE 4

Oxidation of Formaldehyde on Vanadium Catalyst (V_2O_5) at 400°

Experimental conditions		Initial mixture (vol. %)		Reaction products (vol. %)					Yield of products (mol.%)*			% conversion of HCOH
flow rate (liters/hr)	contact time (sec.)	HCOH	O_2	acids	aldehydes	CO_2	CO	O_2	acids	CO_2	CO	
29	1.2	2.0	1.6	0.04	0.25	1.2	0.8	0	2.3	68.5	45.6	87
31	1.1	2.1	1.6	0.03	0.27	1.0	0.8	0	1.6	54.6	43.6	87
35	1.0	2.2	21.0	0.03	0.05	1.4	0.8	16.4	1.4	65	37.3	98

As can be seen from the data of Table 4, formaldehyde is about 87-98% converted at 400° and for a contact time of about 1 second; traces of acids (0.03 vol. %) were found in the reaction products, a small residue of non-oxidized formaldehyde (0.05-0.27 vol. %), and large amounts of CO_2 and CO. Thus, formaldehyde on vanadium catalyst is not stable in the presence of oxygen. The experiment with acetaldehyde carried out under the same conditions on vanadium catalyst gave the same results.

Experiments with acetic acid gave even higher percent conversion. The results obtained here are given in Table 5.

TABLE 5

Oxidation of Acetic Acid on Vanadium Catalyst (V_2O_5) at 400°, flow rate being 29 l./hr., contact time, 1.2 seconds

Initial mixture (in vol. %)		Reaction products (in vol. %)				Percent conversion
CH_3COOH	O_2	CH_3COOH	CO_2	CO	O_2	
2.0	0.4	0.06	2.2	0.02	0	97
2.1	1.6	0.05	1.8	0.02	0	98
2.3	1.6	0.07	2.6	0.02	0	97
2.0	21.0	0.06	2.2	1.2	17.6	97

As with aldehydes, acetic acid is unstable over vanadium catalyst in the presence of oxygen, and is 97-98% converted to carbon dioxide and carbon monoxide. The carbon balance forces us to assume that with insufficient oxygen (first three experiments) there is evidently also formed methane, determination of which was not carried out.

DISCUSSION OF RESULTS

Investigations of the authors have indicated the existence of qualitative differences in oxidation of propylene on silver and on vanadium oxide preparations studied. Reaction on silver begins at a considerably lower temperature, and proceeds almost to completion, with conversion of all three carbon atoms of each propylene molecule to carbon dioxide. From the products of incomplete oxidation, propylene oxide is found only in traces. Qualitative tests for aldehydes and carboxylic acids were negative. Taking into account the sensitivities of the analytical

* Relative to theoretical yield calculated on the basis of reacted formaldehyde. The sum of reaction products is not equal to 100% due to inaccuracy of the gas analysis.

methods, and the approximate propylene oxide content and upper limits of concentrations of aldehydes and acids, evaluation of the reaction products, expressed in volume percent, gave: propylene oxide about 0.1, aldehydes less than 0.001, carboxylic acids less than 0.001.

It is not clear whether the presence of traces of propylene oxide is due to slowness in its formation process from propylene, or whether propylene oxide forms with equal ease from propylene as ethylene oxide is formed from ethylene, but unlike the latter is too rapidly oxidized to carbon dioxide.

Upon oxidizing propylene on vanadium catalyst, the mole yield with respect to theory constitutes from 41.7 to 66.6% for carbon dioxide, and from 22.2 to 55.5% for carbon monoxide, calculating on the basis of propylene oxidized. A comparison of these data with the mole yield of carbon dioxide and carbon monoxide by oxidation of formaldehyde and acetic acid (Tables 4 and 5) makes it possible to assume that carbon dioxide and carbon monoxide are secondary products, formed principally because of oxidation of intermediate, readily oxidizable products.

Taking into account the high percentage conversion of aldehydes and acids on vanadium catalyst, it can be considered that the small concentrations of aldehydes and acids among the propylene oxidation products observed in the experiments can represent final concentrations of these substances formed by oxidation.

Comparisons of the carbon dioxide to carbon monoxide ratio, formed by oxidation of oxygen-containing organic compounds and propylene, makes possible an orientative evaluation of the possibility for direct propylene oxidation to final products, and subsequent oxidation through a stage of formation of intermediate products, in the vein of the Twigg [3, 4] scheme, which has been proposed by him for ethylene oxidation.

It appears possible that oxidation of propylene on vanadium under the authors' conditions proceeds mainly via the formation of unstable intermediates, which can be further oxidized at a high rate to carbon dioxide and carbon monoxide.

The ease of oxidation of aldehydes and acids may be the cause of low yields for readily-oxidizable products. The ratio of oxidation rates on vanadium catalyst for propylene used on the one hand by the authors, and that of formaldehyde, acetaldehyde and acetic acid on the other, excludes the possibility of attaining high yields of intermediate products. Yields, on hydrocarbon oxidized, can be increased by decrease in contact time, but the volume percentages are then decreased even more. In varying external conditions, the authors failed to change the unfavorable ratio of oxidation rates. This situation appears, as the authors see it, to be one of the possible causes for lack of success by other authors in their attempts to obtain aldehydes and carboxylic acids in adequate amounts by oxidation of unsaturated gases on vanadium catalyst. In order to obtain positive results, catalysts possessing considerably different ratios between oxidation rates of hydrocarbons and oxygen-containing compounds are necessary.

SUMMARY

1. Oxidation of propylene by oxygen of the air on silver catalyst proceeds almost to completion with conversion of all three carbon atoms of propylene to carbon dioxide.

2. Oxidation of propylene over vanadium pentoxide catalyst is accompanied by formation of carbon dioxide and carbon monoxide in considerable amounts and small amounts of aldehydes and carboxylic acids.

3. For the catalysts studied, there occurs an unfavorable ratio of rates of propylene oxidation on the one hand for accumulation of readily-formed oxidation products, and aldehydes and acetic acid on the other.

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BROMINATION OF UNSATURATED COMPOUNDS

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Results of work on bromination of unsaturated compounds by means of complexly-bound bromine are given in the present work. Dioxan dibromide and pyridine dibromide were used as brominating agents. The first complex, described for the first time by Favorsky [1], was proposed by Yanovskaya [2] for the bromination of polyhydroxy phenols, aldehydes and ketones, and other readily-converting compounds. Dioxan dibromide was utilized by Terentyev, Kostov, Yurkevich and Khaskina [3] for bromination of vinyl acetate, whereby the 1,2-dibromoester of acetic acid resulted in 50% yield. Pyridine bromide was used [4] for addition of bromine at the double bond of safrole, p-methoxy-ω-nitrostyrene, and 3,4-methylenedihydroxy-ω-nitrostyrene, which forms only polybromides, with halogen in the ring, upon bromination in the usual manner with bromine in solvent.

The authors used dioxan dibromide for bromination of styrene, hexadiene-2,4, isoprene, acrolein, acrylonitrile, methacrylic acid and vinyl acetate, and in addition, bromination of styrene, isoprene and methacrylic acid by pyridine dibromide.

Reaction, as a rule, was carried out without solvent, and with gentle cooling of the reaction mixture with water. Addition took place in all cases. It was established in experiments with styrene that vinyl substitution (in the side chain) proceeds negligibly. Somewhat lower yields of bromination products are obtained with pyridine dibromide than with dioxan dibromide. Isolation and purification of final substances are extremely simple: the reaction mixture is treated with water and then extracted with ether. After drying the ether layer, the bromoderivative is separated by fractionation.

Thus, dioxan dibromide is found to be a convenient reagent for addition of bromine to various unsaturated compounds.

EXPERIMENTAL*

Bromination of styrene. 25 g (0.1 mole) of dioxan dibromide was added in portions to 10.4 g (0.1 mole) of styrene. Instantaneous decoloration was observed, and moderate heat evolution. The dibromide was precipitated with water, separated, washed well and dried in air. Yield of dibromide was quantitative – 26.4 g; m.p. was 73-74° (from dilute alcohol). A sample mixed with sample of dibromostyrene did not show depression in melting temperature.

Bromination of styrene with pyridine bromide. 2.6 g (0.025 mole) of styrene was added in small portions, with cooling and stirring, to 6 g (0.025 mole) of pyridine bromide dissolved in 20 ml of dichloroethane. Upon addition of the last portion of styrene, the red pyridine dibromide became decolorized. 25 ml of water was then added and titrated with 0.1 N NaOH solution in the presence of methyl orange. 40 ml of alkali was used for the titration. The resulting crystals were washed with water and dried m.p. was 73°. The yield of dibromostyrene was 4.7 g (about 70%). Recalculation of the alkali used for titration of the HBr indicated that the substitution reaction used 7.8% of the bromine in pyridine dibromide.

Bromination of hexadiene-2,4 with dioxan dibromide. 25 g (0.1 mole) of dioxan dibromide (with stirring and ice-cooling) was added in small portions to 11.8 ml (0.1 mole) of hexadiene-2,4 (b.p. 80-81°; n_D^{20} 1.4385; d_4^{20} 0.711), placed in a flask with ground stopper. The reaction mixture was treated and washed with ice water, after which it was extracted with ether. The ether extract was dried with calcium chloride, and after distilling off the ether, the substance was redistilled in vacuo. The main part distilled at 86-88° (11 mm). Yield was 15.2 g (86% of theory), calculating on the basis of dibromohexane; a yellow-brown oil with sharp odor and lachrymatory action, decolorizing bromine water and potassium permanganate, had d_4^{20} 1.632 and n_D^{20} 1.5335, which is in full agreement with the literature data for 2,5-dibromohexene-3, [5].

0.1956 g sub.: 0.3025 g AgBr. Found %: Br 65.82; M (cryoscopically in benzene) 240.35. $C_6H_{10}Br_2$. Calculated %: Br 66.05; M 241.97.

* The experimental part was carried out with the participation of R. I. Abramovich.

Bromination of isoprene. 2.5 g (0.037 mole) of isoprene (b.p. 34°, d_4^{20} 0.6805, n_D^{20} 1.4215) was brominated with 17.6 g (0.073 mole) of dioxan dibromide. A heavy, yellow-brown oil resulting from treatment of the reaction mixture was obtained. After distillation in vacuo 12.7 g (89.3%) of colorless liquid resulted, with b.p. 32-32.5° (6 mm), d_4^{20} 1.548, n_D^{20} 1.5070.

0.1842 g sub.: 0.3566 g AgBr. Found %: Br 82.35; M (cryoscopically in benzene) 383.15. $C_5H_8Br_4$. Calculated %: Br 82.43; M 387.78.

30.6 g (76.3%) of the tetrabromide was obtained from 7.3 g (0.073 mole) of isoprene and 35.1 g (0.146 mole) of pyridine dibromide, possessing the same physico-chemical and analytical data.

Bromination of acrolein with dioxan dibromide. 7.1 ml (0.107 mole) of freshly distilled acrolein (b.p. 52°) was brominated, with continuous cooling and stirring, by 26.6 g (0.107 mole) of dioxan dibromide. The reaction mixture was treated with ice water and extracted with ether. The ether extract was dried with calcium chloride. After distilling off the ether, the residue was fractionated in vacuo. 16.7 g (72%) of colorless oil with sharp odor and lachrymatory properties, and a b.p. of 79-80° (14 mm) d_4^{20} 2.192, n_D^{20} 1.5082, these constants corresponding to the literature data for dibromopropionic aldehyde [6]. The dibromide did not decolorize bromine water or potassium permanganate. Addition of 2-3 drops of the substance to fuchsin—sulfuric acid solution caused appearance of an intense red-violet color, which indicated presence of the aldehyde group.

0.1928 g sub.: 0.3344 g AgBr. Found %: Br 73.83 M 212.62. $C_3H_4OBr_2$. Calculated %: Br 74.03; M 215.89.

Bromination of acrylonitrile. 10 ml (about 0.15 mole) of acrylonitrile (b.p. 73°, n_D^{20} 1.3914) was brominated at room temperature with 37 g (0.15 mole) of dioxan dibromide. Complete decolorization of the reaction mixture resulted after 24 hours. After washing with cold water, 30.5 g (about 95%) of a thick, oily substance was obtained which, after drying with calcium chloride, had a b.p. of 173° and n_D^{20} 1.5580; possessing lacrymatory action.

0.2008 g sub.: 0.3516 g AgBr. Found %: Br 74.51; N (according to Kjeldahl) 7.00; M (according to Rast) 209.6. $C_3H_3NBr_2$. Calculated %: Br 75.07; N 6.58; M 212.89.

Bromination of methacrylic acid. 9.8 ml (about 0.12 mole) of methacrylic acid (m.p. 15-16°, n_D^{20} 1.4312) was brominated at room temperature with 28.8 g (0.12 mole) of dioxan dibromide. Reaction was terminated after 3 hours. At the end of the reaction, the mixture separated into two layers. After treatment with ice water, the heavy oil was extracted with ether. The ether solution was dried with calcium chloride. Having distilled off the ether, the yellow-brown oil was heated again to 103-104° and then transferred to a vacuum desiccator. Colorless crystals separated after 12-15 days, which were pressed out on a porous plate and dried between sheets of filter paper. Yield was about 25.5 g (89% of theory, calculating on the basis of α,β-dibromomethacrylic acid). The crystals which were recrystallized from ether melted at 47°, corresponding to the literature data for α,β-dibromomethacrylic acid [7]. Solutions of the compound did not show reactions for the double bond.

0.1608 g sub.: 0.2451 g AgBr. Found %: Br 64.89; M 247.36. $C_4H_6O_2Br_2$. Calculated %: Br 65.02; M 245.92.

The equivalent amount of 10% potassium hydroxide solution was added to a hot aqueous solution of the dibromo acid. The solution was evaporated to dryness on a water bath, and the resulting potassium salt of 1-methyl-1,2-dibromopropionic acid was dried in a vacuum desiccator.

0.3264 g sub.: 0.1385 g KBr. Found %: K 13.94. $C_4H_5O_2Br_2K$. Calculated %: K 13.77.

4.9 g (0.058 mole) of methacrylic acid was brominated under analogous conditions with 13.8 g (0.058 mole) of pyridine dibromide. After appropriate treatment, 10.9 g (76.7%) of dibromo acid with m.p. 47° was isolated. A sample mixed with the compound synthesized earlier (with dioxan dibromide) did not show depression in melting temperature.

Bromination of methacrylate. 10.5 ml (0.116 mole) of methyl methacrylate (b.p. 80.5°, d_4^{20} 0.950, n_D^{20} 1.3983) was brominated by addition of 28.8 g (0.116 mole) of dioxan dibromide in small portions. The reaction mixture was left overnight until the following day, when it was washed with cold water and treated with ether; the ether extract was dried with calcium chloride. After distilling off the ether, the residue was kept in a vacuum desiccator and then fractionated in vacuo. 27.5 g (95% calculating on the basis of dibromide of methyl propionate) of colorless oil: b.p. 32° (4 mm), d_4^{20} 1.931, n_D^{20} 1.5122. The compound showed no reactions for double bond.

0.2014 g sub.: 0.3073 g AgBr. Found %: Br 64.98; M 247.27. $C_4H_6O_2Br_2$. Calculated %: Br 65.02; M 245.92.

Bromination of vinyl acetate. 10.7 ml (0.116 mole) of vinyl acetate (b.p. 73°, n_D^{20} 1.3958) was brominated with 28.8 g (0.116 mole) of dioxan dibromide, with stirring and cooling, with strong heat evolution and rapid

decolorization. The brown reaction mixture was poured into ice water, the heavy oil washed several times with water, dried with calcium chloride, and distilled in vacuo. 22.5 g (78%) of colorless, gradually-yellowing oil was obtained with b.p. 70-72.5° (2 mm), d_4^{20} 1.918, n_D^{20} 1.5052. Possessing a lachrymatory action. Did not decolorize potassium permanganate or bromine water.

0.1734 g sub.: 0.2637 g AgBr. Found %: Br 64.73 M 241.44. $C_4H_6O_2Br_2$. Calculated %: Br 65.02; M 245.92.

SUMMARY

A new method for bromination of an unsaturated compound with dioxan dibromide has been proposed.

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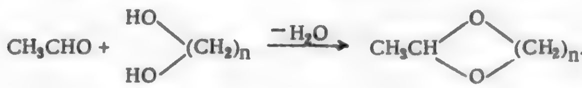
A METHOD FOR SYNTHESIS OF CYCLIC ACETALDEHYDEACETALS

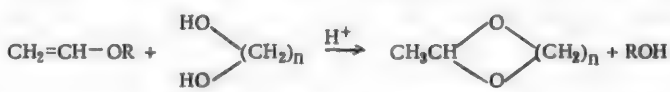
M. G. Voronkov and E. S. Titlinova

Up to the present time, the principal method for synthesis of cyclic acetaldehydeacetals (2-methyl-1,3-dioxacycloalkanes) has been the condensation of acetaldehyde with glycols [1-6], according to the scheme:

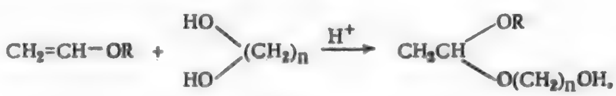


These compounds have also been obtained by reacting acetylene with glycols in the presence of mercury catalysts [7-10], and by transesterification of acetaldehydeacetals [11, 12].

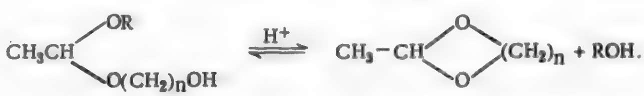
In 1948, the authors proposed a synthetic method for acetaldehydeacetals from vinyl ethylate and alcohols [13]. In the present work, the indicated reaction has been used for the synthesis of cyclic acetaldehydeacetals through the interaction of vinylalkyl esters with glycol, proceeding according to the general scheme:



Reaction proceeds through the stage of formation of mixed acetal



which, under the conditions of synthesis, is intramolecularly esterified



This intramolecular transesterification is readily shifted to the right by distillation of the resulting acetal from the reaction mixture, if it has a lower boiling point than the alcohol forming, or in the contrary case, by distilling off the alcohol which splits out. Thus, it is possible to obtain easily and smoothly cyclic acetaldehyde-acetals by interacting the corresponding glycols with vinyl esters of these alcohols, which have a boiling point sufficiently different from the boiling point of the forming acetal, in order that they may be capable of separation by distillation. For this purpose, a sufficiently practical application can be made only for the two most accessible vinylalkyl esters — vinylethyl ester and vinylbutyl ester.

Synthesis of cyclic acetals by the proposed method is realized by simple distillation on a column of the corresponding vinylalkyl ester and glycol mixture in the presence of 1-3 drops of concentrated HCl. Reaction proceeds with both α- and β-, as well as γ-glycols. By this procedure, the authors obtained two acetals with a seven-membered ring. The yields of cyclic acetaldehydeacetals amounted to 60-90% of theory, calculating on the basis of initial vinylalkyl ester. The acetals obtained, their physical constants, and analytical data are given in Table 1.

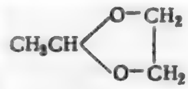
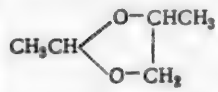
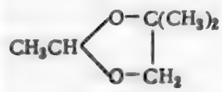
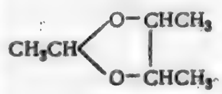
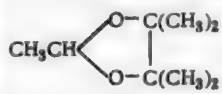
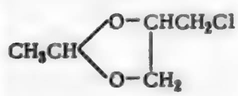
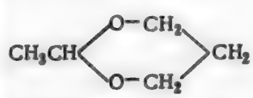
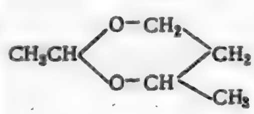
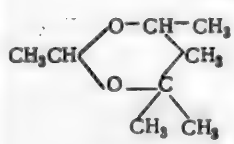
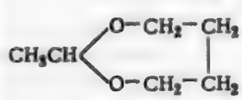
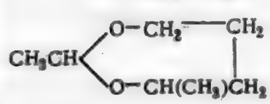
Analysis of the cyclic acetals was carried out according to the method of hydrolytic oximation [14]. Determinations were carried out in sealed tubes which were heated on a water bath for 3-10 hours.

EXPERIMENTAL

The vinylethyl ester and vinylbutyl ester were purified by the method described earlier [15]. All of the initial glycols were purified by distillation on a column with 15 theoretical plates effectiveness. Their physical constants and analytical data are given in Table 2.

TABLE 1

Cyclic Acetaldehydeacetals

Acetal	Formula	Boiling point under pressure (mm)	d_4^{20}	n_D^{20}
2-Methyl-1,3-dioxolane		82.3° (749)	0.9804	1.39705
2,4-Dimethyl-1,3-dioxolane		93.0 (755)	0.9283	1.3949
2,4,4-Trimethyl-1,3-dioxolane*		100.1 (762)	0.8916	1.3938
2,4,5-Trimethyl-1,3-dioxolane		108.5 (752)	0.9117	1.3998
2,4,4,5,5-Pentamethyl-1,3-dioxolane		134.8 (758)	0.8997	1.4121
2-Methyl-4-chloromethyl-1,3-dioxolane		148.5 (765)	1.1531	1.4397
2-Methyl-1,3-dioxane		110.4 (756)	0.9701	1.41394**
2,4-Dimethyl-1,3-dioxane		118.2 (740)	0.9354	1.4140
2,4,4,6-Tetramethyl-1,3-dioxane*		140.0 (766)	0.9039	1.4202
2-Methyl-1,3-dioxephane		127.5 (757)	0.9631	1.4260
2,4-Dimethyl-1,3-dioxephane*		138.0 (762)	0.9319	1.4233

* Synthesized for the first time.

** n_C^{20} 1.41194 n_F^{20} 1.41878.

*** Crude product.

TABLE 1 (Continued)

$n_F^{20}-n_C^{20}$	MR_D		Analysis				Acetal content according to analysis (in %) ± 0.9%	Yield (in %)***
	found	calculated	calculated %		found %			
			C	H	C	H		
0.00668	21.64	21.76	54.53	9.15	54.42, 54.64	9.23, 9.32	99.8	87
0.0067	26.37	26.38	58.80	9.87	58.85, 58.73	9.90, 9.95	99.5	60
0.0066	31.15	30.99	62.04	10.41	62.26, 62.00	10.44, 10.49	99.0	70
0.0068	30.87	30.99	62.04	10.41	62.15, 62.19	10.40, 10.45	99.2	65
0.0070	39.89	40.23	66.63	11.18	66.25, 66.32	11.13, 11.18	99.6	60
0.0075	31.20	31.24	43.97	6.64	–	–	99.2	65
0.00684	26.30	26.38	58.80	9.87	58.60, 59.03	9.90, 9.65	99.8	92
0.0069	31.03	30.99	62.04	10.41	61.97, 61.80	10.38, 10.43	99.4	66
0.0070	40.39	40.23	66.63	11.18	66.49, 36.37	11.01, 11.11	99.6	71
0.0072	30.90	30.99	62.04	10.41	62.30, 62.37	10.39, 10.48	99.4	65
0.0071	35.60	35.61	64.58	10.84	64.42, 64.50	10.80, 10.75	99.4	70

Since the procedures for all of the syntheses were standard, the authors, therefore, have limited themselves to quotation of but a few experiments.

Synthesis of 2-methyl-1,3-dioxolane. (2-Methyl-1,3-dioxacyclopentane). 124 g (2 moles) of ethylene glycol, 180 g (1.8 moles) of vinylbutyl ester and several drops of hydrochloric acid were placed in a distilling flask and distillation column with 15 plates theoretical effectiveness.*

The reaction mixture was heated to boiling with complete return on the column in 30 minutes, after which it was distilled. Yield of 2-methyl-1,3-dioxolane with b.p. 81.5-82.5° was 138.2 g (87% of theory, calculating on the basis of initial vinylbutyl ester). Along with this, there was formed 131 g of butyl alcohol with b.p. 117.0-117.1°.

After a second distillation on the column, the 2-methyl-1,3-dioxolane had the constants given in Table 1.

TABLE 2

Physical Properties of the Initial Glycols

Formula	Boiling point under pressure (in mm)		d_4^{20}	n_D^{20}
$HOCH_2CH_2OH$	197.4	(760)	1.1132	1.4318
$HOCH_2CH_2CH_2OH$	214.5	(737)	1.0539	1.4390
$CH_3CH(OH)CH_2OH$	188.0	(768)	1.0379	1.4325
$HOCH_2CH_2CH_2CH_2OH$	228.0	(763)	1.0190	1.4458
$CH_3CH(OH)CH_2CH_2OH$	207.4	(759)	1.0049	1.4399
$CH_3CH_2CH(OH)CH_2OH$	190.9	(766)	1.0026	1.4379
$CH_3CH(OH)CH(OH)CH_3$	182.0	(758)	0.9870 (25°)	1.4307 (25°)
$(CH_3)_2C(OH)CH_2OH$	175.8	(748)	0.9967	1.4360
$CH_3CH(OH)CH_2CH_2CH_2OH$	221.5	(757)	0.9885	1.4470
$(CH_3)_2C(OH)C(OH)(CH_3)_2$	173.0	(762)	–	1.4326 (45°)
$(CH_3)_2C(OH)CH_2CH(OH)CH_3$	194.2	(752)	0.9239	1.4284
$ClCH_2CH(OH)CH_2OH$	113.0	(10)	1.3226	1.4797

Synthesis of 2-methyl-1,3-dioxane (2-methyl-1,3-dioxacyclohexane). 2 drops of concentrated HCl was added to a mixture of 36.1 g (0.5 mole) of vinylethyl ester and 61 g (0.8 mole) of trimethyleneglycol. The mixture was boiled for 15 minutes and distilled on a column. 24.0 g of ethyl alcohol with b.p. 78.5-78.6° and 47.0 g of 2-methyl-1,3-dioxane with b.p. 105.0-109.2° was obtained. The yield was 92% of theory. After treating with sodium in the cold, and distilling on the column, the compound had the constants given in Table 1.

Synthesis of 2,4-dimethyl-1,3-dioxephane (2,4-dimethyl-1,3-dioxacycloheptane). 3 drops of concentrated HCl was added to a mixture of 36.1 g (0.5 mole) of vinylethyl ester and 52 g (0.5 mole) of 1,4-pentandiol, and the mixture then distilled on the column. 20.2 g of ethyl alcohol of b.p. 77.0-78.9° and 45.6 g (70%) of 2,4-dimethyl-1,3-dioxephane with b.p. 135.5-138°. After a second distillation on the column, the compound had the constants given in Table 1.

All remaining acetals were synthesized by similar procedure from vinylethyl ester and the corresponding glycols.

SUMMARY

A method for synthesis of cyclic acetaldehydeacetals (2-methyl-1,3-dioxacycloalkanes) from vinylalkyl esters and glycols has been developed. According to this method, 11 acetaldehydeacetals with 5-, 6- and 7-membered rings (4 of them synthesized for the first time) have been obtained.

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* In all experiments, upon addition of the catalyst to vinyl ester and glycol, there were usually formed two immiscible layers and intensive exothermic reaction took place, which resulted in miscibility of the layers.

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INVESTIGATIONS IN THE FIELD OF ALKANOSULFONIC ACIDS

XI. INTERACTION OF ALKANOSULFONYL CHLORIDES WITH p-CHLOROANILINE AND p-NITROANILINE

A. G. Kostsova

Reactions of alkanosulfonyl chlorides with aniline were described earlier by the author [1]. The present work had for its aim the problem of studying reactions of the above-mentioned sulfonyl chlorides with p-chloroaniline and p-nitroaniline. It was of interest in this respect to study the effect of the chlorine and of nitro group in a position para to the NH_2 group, upon the course of reaction and the properties of the resulting products.

The reaction with p-chloroaniline was carried out under the same conditions as with aniline, i.e., in ether medium with heating on a water bath. The experiments indicated that chlorine present in a position para to the NH_2 group does not affect markedly the course of the reaction, or the yields of p-chloroanilides, but does affect noticeably their physical properties, in particular, their melting temperatures, which, as a rule, increase sharply as compared with the corresponding unsubstituted anilides (see Table).

An exception to this general rule, to some degree, is the 2-methylethanesulfonyl-p-chloroanilide, whose melting point increases negligibly as compared with the anilide of the same sulfonic acid.

p-Chloroanilides and the unsubstituted anilides are white, crystalline compounds, readily soluble in alkalies, but their alkaline solutions are more difficult to methylate with methyl iodide as compared with the unsubstituted anilides. Thus, upon methylating p-chloroanilides prepared by the authors, the methyl derivatives of butan- and 2-methylbutan-p-chloroanilide, could be isolated in the form of crystalline powders, but their crystallization proceeded very slowly. The remaining p-chloroanilides became methylated only with great difficultly, even upon contact with methyl iodide for many days.

The products of methylation in this case resulted as oily traces on the surface of the alkaline solution, and to isolate, purify and characterize them, did not seem feasible. Methylation of alkansulfonyl-p-chloroanilides proceeds according to the general equation:

$$RSO_2NHC_6H_4Cl + CH_3I + NaOH \longrightarrow RSO_2N(CH_3)C_6H_4Cl + NaI + H_2O.$$

Reaction of alkanosulfonyl chlorides with p-nitroaniline was carried out in pyridine medium while heating on a water bath. In this case, reaction proceeds very slowly. The reaction products — alkanosulfonyl-p-nitroanilides, are formed in negligible yield as a rule; 2-methylethane-, 2-methylpropane- and phenylmethanesulfonyl chloride do not react on the whole with p-nitroaniline under the conditions indicated.

Thus, with p-nitroaniline, the reaction course differs noticeably from that for unsubstituted aniline. The alkanosulfonyl-p-nitroanilides formed, in contrast to p-nitroaniline itself, are in the form of colorless compounds, but when dissolved in alkali, in which they are poorly soluble, it should be mentioned that the anilides and p-chloroanilides produce yellow solutions, while, when dissolved in boiling water, they produce colorless solutions, which prompts one to make the assumption that their sodium salts are colored.

Alkanosulfonyl-p-nitroanilides, in distinction to other N-arylamides described in the authors [1], are poorly soluble in alcohol. Alcoholic solutions, like N-arylamides, are readily precipitated by water.

The reaction of methanesulfonyl chloride with m-nitroaniline was also studied by the authors. There were no profound differences in reaction with p-nitroaniline for the given case. The reaction product was formed in small amount as colorless crystals; its alkaline solutions are also yellow in color, and the aqueous solutions colorless.

The melting points of alkanosulfonyl-p-nitroanilides are, as a rule, higher than for alkanosulfonyl-p-chloroanilides, and the melting points of the latter are higher than for unsubstituted alkanosulfonylanilides (see Table).

TABLE

Melting Points of Anilides: The p-Chloro- and p-Nitroanilides of Alkanosulfonyl Acids

Alkanosulfonylanilides	M.p.	Alkanosulfonyl-p-chloroanilides	M.p.	Alkanosulfonyl-p-nitroanilides	M.p.
$CH_3SO_2NHC_6H_5$	99°	$CH_3SO_2NHC_6H_4Cl$	148°	$CH_3SO_2NHC_6H_4NO_2$.	183°
$C_2H_5SO_2NHC_6H_5$	55	$C_2H_5SO_2NHC_6H_4Cl$.	121	$C_2H_5SO_2NHC_6H_4NO_2$	162
iso-$C_3H_7SO_2NHC_6H_5$. .	84	iso-$C_3H_7SO_2NHC_6H_4Cl$	87	—	—
n-$C_4H_9SO_2NHC_6H_5$. . .	35	n-$C_4H_9SO_2NHC_6H_4Cl$	62	n-$C_4H_9SO_2NHC_6H_4NO_2$	91
iso-$C_5H_{11}SO_2NHC_6H_5$.	42	iso-$C_5H_{11}SO_2NHC_6H_4Cl$.	61	iso-$C_5H_{11}SO_2NHC_6H_4NO_2$	112

EXPERIMENTAL *

p-Chloroaniline, with m.p. 70-71°, chemically-pure, was used for the reaction. p-Nitroaniline had a m.p. of 146-147°. All alkanosulfonyl-p-chloroanilides were obtained according to the same procedure and, therefore, a detailed account is given only for the first representative.

A description and the procedure for alkanosulfonyl-p-nitroanilide are also given.

1. Synthesis of methanesulfonyl-p-chloroanilide. 2 g of methanesulfonyl chloride in 30 ml of anhydrous ether and 4.4 g of p-chloroaniline were heated on a water bath at 40-45° under reflux for 1.5-2 hours. After termination of heating, the reaction mixture was left to the following day; the p-chloroaniline hydrochloride which resulted from the reaction was separated, the ether filtrate evaporated or distilled off on a water bath. The solid yellow precipitate was treated with 5% alkali. The portion which did not dissolve was separated, and the alkaline solution was acidified with dilute hydrochloric acid to a stable turbidity, from which, when cooled with ice, and rubbing with a glass rod, fine white crystals of methanesulfonyl-p-chloroanilide precipitated. The precipitate was isolated and dried. The yield was 2 g (55.5%). Recrystallized from alcohol and water; soluble in organic solvents (alcohol, ether, acetone and others), poorly soluble in water.

0.1012 g sub.: 4.95 ml 0.1 N H_2SO_4. 0.095 g sub.: 0.1090 g $BaSO_4$. Found %: N 6.84; S 15.73.
$C_7H_8O_2NSCl$. Calculated %: N 6.82; S 15.60.

2. Synthesis of ethanesulfonyl-p-chloroanilide. 1 g of ethanesulfonylchloride, 1.98 g of p-chloroaniline and 20 ml of anhydrous ether were taken. The yield of ethanesulfonyl-p-chloroanilide was 1.24 g (73%). Recrystallized from alcohol and water. White, fine, fluffy crystals.

0.1182 g sub.: 5.29 ml 0.1 N H_2SO_4. 0.1328 g sub.: 0.1384 g $BaSO_4$. Found %: N 6.26; S 14.29.
$C_8H_{10}O_2NSCl$. Calculated %: N 6.30; S 14.50.

3. Synthesis of 2-methylethanesulfonyl-p-chloroanilide. 2 g of 2-methylethanesulfonyl chloride, and 4 g of p-chloroaniline, in 30 ml of anhydrous ether were taken. The yield of 3-methylethanesulfonyl-p-chloroanilide was 1.3 g (40.6%).

0.1284 g sub.: 0.24 ml 0.1 N H_2SO_4. 0.1512 g sub.: 0.1514 g $BaSO_4$. Found %: N 5.71; S 13.72.
$C_9H_{12}O_2NSCl$. Calculated %: N 5.99; S 13.70.

4. Synthesis of butanesulfonyl-p-chloroanilide. 1 g of butanesulfonyl chloride, and 1.73 g of p-chloroaniline, in 20 ml of anhydrous ether, were taken. The yield of butanesulfonyl-p-chloroanilide was 1 g (56.8%). Slightly yellowish, fine crystals.

0.0991 g sub.: 3.98 ml 0.1 N H_2SO_4. 0.1420 g sub.: 0.1330 g $BaSO_4$. Found %: N 5.62; S 12.84.
$C_{10}H_{14}O_2NSCl$. Calculated %: N 5.65; S 12.92.

5. Synthesis of 2-methylbutanesulfonyl-p-chloroanilide. 1 g of 2-methylbutanesulfonyl chloride and 1.5 g of p-chloroaniline, in 20 ml of anhydrous ether, were taken. The yield of 2-methylbutanesulfonyl-p-chloroanilide was 0.77 g (50.3%).

0.0350 g sub.: 1.22 ml 0.1 N H_2SO_4. 0.0740 g sub.: 0.0670 g $BaSO_4$. Found %: N 4.88; S 12.41.
$C_{11}H_{16}O_2NSCl$. Calculated %: N 5.35; S 12.23.

6. Methylation of butanesulfonyl-p-chloroanilide. 0.2 g of butanesulfonyl-p-chloroanilide was dissolved in a small amount of 7 % caustic alkali (the alkali being added dropwise to p-chloroaniline to dissolution). 0.6 g of methyl iodide (four-fold excess over the calculated) was added to the alkaline solution. The resulting emulsion

* L. D. Yakimova and V. D. Levitan participated in the experimental work.

was heated on a round-bottomed flask with reflux condenser, on a water bath at 45-50° for 40-45 minutes. The flask with reaction mixture was then left standing for 24 hours, and the flask contents then transferred to a Petri dish for evaporation of the excess methyl iodide. Oily spots remained on the surface of the alkaline solution, which upon prolonged rubbing with a glass rod, crystallized. The crystals were separated from the alkaline solution and washed with water on a filter. The yield was 1.8 g (90%). It was recrystallized from alcohol and water. The m.p. was 59°. Butanesulfonyl-N-methyl-p-chloroaniline is insoluble in alkali, and in water, readily soluble in alcohol, ether, benzene and acetone.

0.081 g sub.: 3.15 ml 0.1 N H_2SO_4. Found %: N 5.44. $C_{11}H_{16}O_2NSCl$. Calculated %: N 5.35.

7. Methylation of 2-methylbutanesulfonyl-p-chloroanilide. 0.2 g of 2-methylbutanesulfonyl-p-chloroanilide in 5 ml of 6% alkali and 0.44 g of methyl iodide were taken. Procedure was analogous to the preceeding. Yield was 0.17 g (81%). 2-Methylbutanesulfonyl-N-methyl-p-chloroanilide: colorless, fine crystals with m.p. 54-55°.

0.0436 g sub.: 1.56 ml 0.1 N H_2SO_4. Found %: N 5.00. $C_{12}H_{18}O_2NSCl$. Calculated %: N 5.08.

8. Synthesis of methylanesulfonyl-p-nitroanilide. 1.5 g of methanesulfonyl chloride was added to 1.8 g of p-nitroaniline which was dissolved in 10 ml of pyridine. Spontaneous evolution of heat from the reaction mixture at 20-25° was observed. To complete reaction, the mixture was heated on a water bath with reflux condenser at 60-70° for 1-1.5 hours, and then left to stand for 24 hours. The transparent, dark-brown pyridine solution was precipitated with cold water, and acidified with hydrochloric acid. An orange-red precipitate separated, representing a mixture of unreacted p-nitroaniline and the product of reaction, methanesulfonyl-p-nitroanilide. The latter was isolated when treated with alkali in which it dissolved while the p-nitroaniline did not dissolve. The methanesulfonyl-p-nitroanilide was precipitated from the alkaline extract with dilute sulfuric acid. Treatment with alkali was repeatedly carried out. The methanesulfonyl-p-nitroanilide precipitated out in the form of fine, fluffy, creamy crystals from the acidified solution. Their second dissolution in alkali and subsequent precipitation with acid, or recrystallization from alcohol and water, resulted in colorless crystals. The yield was 0.4 g (14.3%).

0.075 g sub.: 6.91 ml 0.1 N H_2SO_4. Found %: N 12.89. $C_7H_8O_4N_2S$. Calculated %: N 12.96.

9. Synthesis of ethanesulfonyl-p-nitroanilide. 1 g of ethanesulfonylchloride and 1 g of p-nitroaniline in 6 ml of pyridine were taken. Yield of ethanesulfonyl-p-nitroanilide was 0.2 g (11.1%). Fine, colorless, fluffy crystals.

0.053 g sub.: 4.58 ml 0.1 N H_2SO_4. Found %: N 12.09. $C_8H_{10}O_4N_2S$. Calculated %: N 12.18.

10. Synthesis of butanesulfonyl-p-nitroanilide. 1 g of butanesulfonyl chloride and 0.9 g of p-nitroaniline dissolved in 6 ml of pyridine were used. Yield of the butanesulfonyl-p-nitroanilide was 0.1 g (6%). The reaction product was at first a yellowish-pink and after two purifications by dissolution in alkali, and precipitation with acid, became completely colorless.

0.060 g sub.: 4.55 ml 0.1 N H_2SO_4. Found %: N 10.61. $C_{10}H_{14}O_4N_2S$, Calculated %: N 10.85.

11. Synthesis of 2-methylbutanesulfonyl-p-nitroanilide. 1.35 g of 2-methylbutanesulfonyl chloride and 1.1 g of p-nitroaniline in 7 ml of pyridine were used. The yield of 2-methylbutanesulfonyl-p-nitroanilide was 0.11 g (5%). 0.7 g, i.e., over 50% of the p-nitroaniline, which was taken for reaction and did not react, was isolated. The reaction product was recrystallized from alcohol and water.

0.068 g sub.: 4.91 ml 0.1 N H_2SO_4. Found %: N 10.10. $C_{11}H_{16}O_4N_2S$. Calculated %: N 10.29.

12. Synthesis of methanesulfonyl-m-nitroanilide. 1.5 g of methanesulfonyl chloride and 1.8 g of m-nitroaniline in 10 ml of pyridine were used for the reaction. The yield of methanesulfonyl-m-nitroanilide was 0.5 g (18%). Slightly-pink-yellow crystals, becoming almost colorless on recrystallizing from alcohol and water, M.p. 164°.

0.081 g sub.: 7.31 ml 0.1 N H_2SO_4. Found %: N 12.63. $C_7H_8O_4N_2S$. Calculated %: N 12.96.

SUMMARY

1. p-Chloroanilides, namely, methane-, ethane-, 2-methylane-, butane- and 2-methylbutanesulfonyl acids, have been synthesized and characterized.

2. It has been demonstrated that butane- and 2-methylbutanesulfonyl-p-chloroanilides are relatively easy to methylate, the lower homologs methylating with greater difficulty.

3. The p-nitroanilides of methane-, ethane, butane- and 2-methylbutanesulfonic acids, and the m-nitroanilide of methanesulfonic acid have been synthesized and characterized.

4. The effects of chlorine and nitro groups in the para position to the NH_2 group upon the reaction course, the melting point, and other properties of the compounds forming, have been demonstrated.

5. The conditions used by the authors for 2-methylethane-, 2-methylpropane - and phenylmethanesulfonyl chlorides, do not apply to p-nitroaniline.

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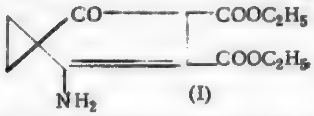
* See Consultants Bureau Translation, page 1477.
** See Consultants Bureau Translation, page 1471.

SPIRO-(2,4)-HEPTANE

Ya. M. Slobodin and M. V. Blinova

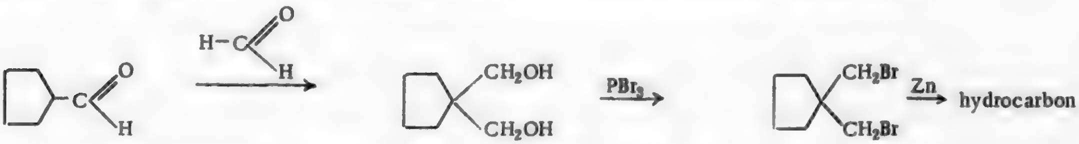
The first attempt to synthesize spiro-(2,4)-heptane was undertaken by Radulescu [1] in 1909 by condensation of the diethyl ester of cyclopropandicarboxylic acid with the diethyl ester of succinic acid, in the presence of sodium ethylate and sodamide. Resulting from the reaction was the formation of spirane (I),



(I)

which failed to convert into the hydrocarbon. There are no other indications in the literature of attempts to synthesize spiroheptane.

In the present investigation, the spiroheptane synthesis was carried out according to the scheme:



1,1-Dimethylolcyclopentane [2] was obtained by condensation of cyclopentylformaldehydewith formaldehyde in alkaline medium, which, upon reaction with PBr_3, was converted into the dibromide, and finally, by reacting the bromide with zinc dust, the hydrocarbon was obtained.

In the dispersion spectrum for the hydrocarbon, a line with frequency of 1650 cm^{-1} was found, a fact which indicates the presence of a hydrocarbon with double bond.

Fractionation of the hydrocarbon on a microcolumn with an effectiveness of 30 theoretical plates, gave two fractions: b.p. 98.6-99.6° and 105.6-106.6°. The low boiling fraction did not represent an individual compound: in its dispersion spectrum, the band at frequency 1650 cm^{-1} was weakened.

To determine the composition and structure of the resulting hydrocarbon mixture, it was ozonized. Upon decomposition of the ozonide with water, an oily layer floated to the top, which was found to be the hydrocarbon.

B.p. 98°; d_4^{20} 0.8203; n_D^{20} 1.43762; MR_D 30.69. C_7H_{12}; calculated 30.83 (increment for three-membered ring 0.7).

There was no maximum in the range 5.95-6.25 μ for the infra-red absorption spectrum of the hydrocarbon, which indicated the absence of a double bond. The manner of synthesis and the physical properties of the hydrocarbon made it possible to attribute to it the structure of spiro-(2,4)-heptane. For comparison, there are given in the table the properties for spiro-(2,4)-heptane and those of its nearest homolog, spiro-(2,5)-octane [3].

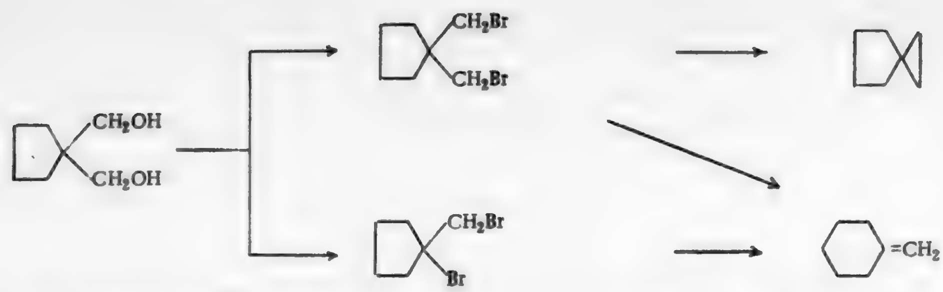
TABLE

Name of hydrocarbon	B.p.	d_4^{20}	n_D^{20}
Spiro-(2,4)-heptane	98°	0.8203	1.4376
Spiro-(2,5)-octane	125.5	0.8282	1.4476

Formic acid and cyclohexanone were found among the decomposition products of the ozonide, which could have been formed as the result of ozonolysis of methylenecyclohexane. For quantitative characterization of the hydrocarbon mixture in the boiling range of 98-101°, it was hydrogenated. The amount of hydrogen absorbed amounted to 48.9%, calculating on the basis of the hydrocarbon, C_7H_{12}, with one double bond. The bromine numbers indicated a somewhat higher degree of unsaturation, evidently related to the ease of rupture of the three-membered ring of spiroheptane.

Thus, from the synthesis, there resulted a hydrocarbon mixture consisting of spiroheptane and methylenecyclohexane.

Formation of methylenecyclohexane was found to be the result of a partial rearrangement, which can occur both during synthesis of the bromide from dimethylolcyclopentane, as well as during synthesis of the hydrocarbon by reaction with zinc bromide in the process of forming,



The expansion of a five-membered ring into a six-membered ring under the influence of chemical reagents has been observed many times. Thus, Nametkin and Morozova [4], by reacting hydrogen halide acids with cyclopentylcarbinol, obtained a mixture of bromomethylcyclopentane and cyclohexyl bromide. Dimethylcyclopentylcarbinol reacted with HBr and converted into a mixture of two bromides, one of which contained the cyclopentane ring, and the other the cyclohexane ring. By reacting dehydrating agents with alcohols containing the cyclopentyl radical, expansion of the five-membered ring into a six-membered ring also took place. Thus, Rozanov [5], by dehydrating cyclopentylcarbinol with oxalic acid, obtained cyclohexene. Nametkin and Gabriadze [6], by dehydrating dimethylcyclopentylcarbinol, observed the formation of two hydrocarbons, one of which contained a five-membered ring, and the second, a six-membered ring.

Data obtained by the authors in the present investigation indicate similarity in synthesis of spiro-(2,4)-heptane with that of other spirane hydrocarbons containing the three-membered ring. Syntheses of all spiranes with three-membered rings are accompanied by expansion of the initial ring,with formation of methylenecyclanes. Thus, closure of a second three-membered ring, in the strained dibromodimethylcyclopropane, leads primarily to expansion of the three-membered ring to a four-membered. There occurs, to a lesser extent, rupture of the ring, with formation of the unsaturated hydrocarbon containing an open chain of carbon atoms. Under the usual conditions, formation of spiropentane does not take place [7].

Closure of the three-membered ring in the less-strained dibromodimethylcyclobutane leads to exapnsion of the four-membered ring to a five-membered ring. Formation of an unsaturated hydrocarbon with an open chain of carbon atoms does not occur. Under normal conditions, spirohexane likewise does not form [8].

Finally, closure of the three-membered ring in unstrained dibromodimethylcyclopentane leads to expansion of the initial five-membered ring into a six-membered ring. At the same time, formation of considerable amounts of spiroheptane was observed.

EXPERIMENTAL

1,1-Dimethylolcyclopentane

Cyclopentylformaldehyde was the initial material used for synthesis of 1,1-dimethylolcyclopentane.

B.p. 40° (17 mm) d_4^{20} 0.9262; n_D^{20} 1.44145. Found %: C 73.32; H 10.24. Calculated %: C 73.47; H 10.20.

Semicarbazone: m.p. 135-137°. Found %: N 27.41. Calculated %: N 27.42.

On storage, the aldehyde polymerized partially. The polymer melted at 117°; M 330. Calculated: $(C_6H_{10}O)_3$ M 228; $(C_6H_{10}O)_4$. M 384.

Literature data for cyclopentylformaldehyde [9, 10]: b.p. 48° (21 mm), 52-53° (24 mm); semicarbazone: m.p. 125°; polymer: m.p. 117-117.5°.

Dispersion Spectrum of the Aldehyde

290 (1), 359 (1), 434 (5), 772 (1), 895 (10), 930 (1), 964 (3), 1012 (4), 1036 (1), 1081 (2), 1098 (3), 1153 (1), 1201 (1), 1300 (2), 1340 (1), 1393 (8), 1451 (10), 1481 (1), 1718 (10), 2868 (15), 2913 (5), 2961 (20 b. db.).

115 g of 30% formalin and 400 ml of water were placed in a flask equipped with stirrer and two dropping funnels, 57 g of cyclopentylformaldehyde was added from one dropping funnel, with vigorous stirring, and from the other was dispensed a suspension made of 26 g $Ca(OH)_2$ in 200 ml of water. Temperature was maintained at 30°. After addition of the reagents, the flask was heated to 50° and kept at this temperature for 1 hour. The mixture was cooled, and the excess $Ca(OH)_2$ filtered off. The filtrate was neutralized and concentrated in vacuo. The crystals which precipitated were filtered off. The diol was extracted with dichloroethane for 5-7 days. After

crystallization from dichloroethane, there was obtained 1,1-dimethylolcyclopentane in high purity. The yield was 86%.

B.p. 91-93°.

Found %: C 64.90; H 10.72. $C_7H_{14}O_2$. Calculated %: C 64.61; H 10.77.

1,1-Dibromodimethylcyclopentane

16.8 g of PBr_3 was placed in a flask, and with ice-water cooling, 10 g of the diol and 2 g of pyridine were introduced in small portions. The mixture was kept for 1 hour at room temperature, and was then heated on a boiling water bath to completion of HBr evolution. The reaction product was poured into cold water, extracted with ether, dried, and distilled. The yield was 40%.

B.p. 122-124° at 15 mm d_4^{20} 1.6644 n_D^{20} 1.5344. MR_D 47.84; calculated 47.85. Found %: Br 62.00. $C_7H_{12}Br_2$. Calculated %: Br 62.50.

Combined Dispersion Spectrum for the Dibromide

238 (4), 310 (1), 335 (1), 437 (4), 453 (2), 473 (1), 558 (2), 591 (3 b), 648 (10 b), 816 (1), 870 (1), 899 (1), 986 (2), 1005 (4), 1201 (2), 1253 (3), 1300 (2), 1351 (3), 1390 (2), 1430 (3), 1453 (6), 2872 (5 b), 2921 (3 b), 2965 (8 b), 3013 (3).

Spiro-(2,4)-heptane

The hydrocarbon was obtained by splitting out bromine with zinc dust from the dibromide in 85% alcohol. The bromide was added slowly from a dropping funnel. The mixture was boiled for 2 hours under reflux. The hydrocarbon was distilled with steam, dried, and distilled over metallic sodium. The yield was 90%.

B.p. 102-107°; d_4^{20} 0.8378; n_D^{20} 1.4510.

Combined Dispersion Spectrum for the Hydrocarbon

264 (2), 346 (1), 402 (3), 442 (3 b), 498 (5 b), 543 (1), 583 (1), 623 (2), 678 (1), 708 (3), 762 (4 b), 894 (3), 952 (10), 976 (2), 1025 (4 b), 1072 (1), 1106 (3), 1144 (2), 1181 (2), 1225 (3), 1271 (2), 1356 (6), 1439 (8), 1650 (5), 2860 (5),2904 (2), 2936 (5), 2961 (5), 2992 (5).

In the second experiment, bromine was split out from the dibromide by means of zinc dust in the presence of sodium carbonate and sodium iodide. The hydrocarbon which resulted in this case hardly differed from the above-described hydrocarbon in its properties and spectrum.

The hydrocarbon was distilled on a microcolumn with an effectiveness of 30 theoretical plates, fractions with b.p. 98.5-99.5° (n_D^{20} 1.43994) and with b.p. 105.5-106.5° (n_D^{20} 1.45257), being isolated. The lower-boiling fraction was rich in spiroheptane. Spectroscopic investigation, however, indicated that it was not free from unsaturated hydrocarbons, although the frequency of the double bond was considerably weakened.

0.5054 g of hydrocarbon were hydrogenated over platinum catalyst. 60.8 ml (18.8°, 772 mm) or 48.9%, calculated on the basis of one double bond reduced.

The bromine number indicated content of unsaturated at 60%.

To determine the nature of the unsaturated hydrocarbon in the resulting mixture, the higher boiling fraction was ozonized. Ozonization was carried out in ethyl chloride. The ozonide was decomposed with water. An oily layer floated to the top, which was found to be the hydrocarbon. Its properties are given above.

After decomposition of the ozonide, alkali titration data indicated an acid content, calculated as formic acid, of 0.788 g. Determination of formic acid according to the calomel method indicated its content to be 0.740 g. Thus, the formic acid content in the ozonolysis products coincided quite well with the total acidity. The alkaline solution was extracted with ether. After removal of the ether, the residue was treated with 2,4-dinitrophenylhydrazine. After one recrystallization from alcohol, the 2,4-dinitrophenylhydrazone melted at 154-155°. A sample mixed with the 2,4-dinitrophenhylhydrazone prepared from pure cyclohexanone, melted without depression at 154-156°.

SUMMARY

1. 1,1-Dimethylolcyclopentane, in 86% yield, has resulted by condensation of cyclopentylformaldehyde with formaldehyde in alkaline medium.

2. Splitting out of bromine from 1,1-dibromodimethylcyclopentane by zinc dust leads to the formation of a hydrocarbon mixture which contains about 40% of spiro-(2,4)-heptane and about 60% methylenecyclohexane.

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CYCLOHEXANONE DERIVATIVES OF MONOSES AND POLYHYDROXY ALCOHOLS

V. F. Kazimirova

Acetone derivatives of monoses and of polyhydroxy alcohols have been described in detail in the literature [1], and have been used for synthesis of other compounds. Cyclohexanone derivatives are encountered less frequently [2] and are less well-known. Dicyclohexylidene-d-xylose, dicyclohexylidene-l-arabinose, dicyclohexylidene-l-sorbose, as well as tricyclohexylidene-mannite, dicyclohexylidene-dulcite and cyclohexylidene-glycerine, described in the present article, were obtained by condensation of monoses and polyhydroxy alcohols with cyclohexanone, in the presence of sulfuric acid.

It is convenient to carry out the reaction in ether, benzene, or petroleum ether solution. Cyclohexanone and concentrated sulfuric acid were added to the monose or alcohol suspension in one of the enumerated solvents; the mixture was stirred, and the cyclohexanone compound which was in process of formation, went into solution, from which, after neutralization, it crystallized out. Crystallization took place quite readily at low temperature. The cyclohexanone compound crystallized well, melted above the corresponding acetone compounds, dissolved readily in ether, benzene, petroleum ether, acetone, alcohol, and other organic solvents, was insoluble in water and volatile with solvent vapors.

EXPERIMENTAL

Dicyclohexylidene-l arabinose. 15 ml of cyclohexanone and 1.5 ml of concentrated sulfuric acid were added to a suspension of 7 g of pure, dry, l-arabinose in 40 ml of ether. The mixture was stirred for 8 hours, and then left for 24 hours. Practically everything dissolved after 2 hours, but if condensation was terminated at this stage, then the yield of dicyclohexylidene-arabinose was lower. The ether layer was separated from the oily layer and neutralized with dry sodium carbonate. After cooling, the solution crystallized. The crystals were separated from the residue by filtration, and purified by recrystallization from petroleum ether. The yield was 6.5 g (46%).

M.p. 73-74°; $[\alpha]^{20} - 4.8°$ in benzene (c 2.159; l 0.9504).

0.1740 g sub.: 0.4190 g CO_2; 0.1317 g H_2O. 0.5320 g sub.: 18.21 g benzene: Δt 0.516°. Found %: C 65.67; H 8.45; M 307. $C_{17}H_{25}O_5$. Calculated %: C 66.80; H 8.38; M 310.

Dicyclohexylidene-d-xylose. Synthesis was carried out in a manner analogous to that for dicyclohexylidene-arabinose. 6.7 g (43%) of dicyclohexylidene-xylose was obtained from 7.5 g of d-xylose. Crystallized from petroleum ether; colorless needles, clustered into nodules; volatile with solvent vapors.

M.p. 102.5-103°; $[\alpha]^{21} + 21.5°$ in benzene (c 2.44; l 0.9504).

0.1348 g sub.: 0.3258 g CO_2; 0.0997 g H_2O. 0.5126 g sub.: 16.80 g benzene: Δt 0.505°. Found %: C 65.91; H 8.28; M 309. $C_{17}H_{26}O_5$. Calculated %: C 65.80; H 8.38; M 310.

Dicyclohexylidene-l-sorbose. 20 ml of cyclohexanone and 3 ml of concentrated sulfuric acid were added to 9 g of pure, dry l-sorbose suspension in 60 ml of petroleum ether. The mixture was stirred for 12 hours and left for 24 hours. 30 ml of petroleum ether was added; neutralization with dry sodium carbonate; filtered. After cooling, a crystalline precipitate separated, which was removed, by filtration, from the yellow syrup and crystallized from petroleum ether. Yield was 5.6 g (42%); volatile with solvent vapors.

M.p. 118-119°; $[\alpha]^{20} - 12.59°$ in benzene (c 2.506; l 0.9504).

15.10 mg sub.: 35.21 mg CO_2; 11.55 mg H_2O. 20.11 mg sub.: 46.98 mg CO_2; 15.34 mg H_2O. 0.4764 g sub.: 16.37 g benzene: Δt 0.44°. Found %: C 63.60, 63.71; H 8.50, 8.48; M 339. $C_{18}H_{28}O_6$. Calculated %: C 63.53; H 8.23; M 340.

Tricyclohexylidene-mannite. A mixture of 10 g of mannite, 50 ml of dry benzene, 30 ml of cyclohexanone and 3.5 ml of concentrated sulfuric acid was stirred for 8 hours and left overnight. The benzene solution was separated from a small oily layer, neutralized with dry sodium carbonate, and filtered. The solvent was evaporated at low temperature. After crystallization from petroleum ether, colorless crystals resulted. Yield was 10 g (58.7%).

M.p. 82-83° $[\alpha]^{20}$ −4.5° in benzene (c 2.55; l 0.9504).

0.1316 g sub.: 0.3301 g CO_2: 0.1072 g H_2O. 0.5208 g sub.: 17.23 g benzene: Δt 0.37°. Found %: C 68.42; H 9.13 M 420. $C_{24}H_{38}O_6$. Calculated %: C 68.24; H 9.05; M 422.

Tricyclohexylidene-mannite dissolves very readily in benzene at room temperature, and it is most convenient to carry out condensation of mannite with cyclohexanone in this solvent.

Dicyclohexylidene-dulcite. 10 g of dulcite, 20 ml of cyclohexanone and 3 ml of concentrated sulfuric acid were stirred for 8 hours and left for 24 hours. The solidified mass was washed thoroughly with water, dilute sodium carbonate solution, and water. Colorless crystals resulted, which were recrystallized from alcohol. The yield was 8.6 g (45%). Melting point of the dry compound was 137°.

14.00 mg sub.: 32.41 mg CO_2; 10.83 mg H_2O. 18.61 mg sub.: 43.00 mg CO_2; 14.76 mg H_2O. 0.22 g sub.: 24.50 g dioxan (K 48): Δt 0.13°. Found %: C 63.18, 63.06; H 8.66, 8.87; M 331. $C_{18}H_{30}O_6$. Calculated %: C 63.15; H 8.77; M 342.

Dicyclohexylidene-sorbite. A viscous oil.

Cyclohexylidene-glycerine. 27 g of pure, anhydrous glycerine, 60 ml of cyclohexanone, 4.5 ml of concentrated sulfuric acid and 75 ml of petroleum ether were stirred for 12 hours and left at room temperature for 48 hours. The ether solution was neutralized with dry sodium carbonate, and the solvent filtered by suction under reduced pressure. The reaction product was distilled two times, b.p. 118-120° at 5 mm. Yield was 22.3 g (44.6%), colorless liquid. soluble in ether, benzene, chloroform, insoluble in water.

n_D^{21} 1.484 d_{20}^{20} 1.0961; d_4^{20} 1.0931.

0.1521 g sub.: 0.3517 g CO_2; 0.1280 g H_2O. Found %: C 63.05; H 9.40. $C_9H_{16}O_3$. Calculated %: C 62.79; H 9.30.

SUMMARY

Well-crystallizing cyclohexlidene derivatives of l-arabinose, d-xylose, l-sorbose, mannite, dulcite and glycerine (liquid), not described in the literature, have been synthesized.

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CONVERSION AND SYNTHESIS OF CARBOHYDRATES

X. SYNTHESIS OF d- AND l-LYXOFLAVINS

V. M. Berezovsky, E. P. Rodionova and L. I. Strelchunas

Of the many flavins which have been synthetically prepared, only some of the simple riboflavin analogs possessed an activity partially equivalent to that for Vitamin B_2, other flavins possessing no vitamin activity at all, or only to a negligible degree. Of the natural flavins, only d-riboflavin was known until very recently; a publication came out not long ago, however, [1], concerning the isolation of l-lyxoflavin from human heart muscle.

Of the stereoisomers of riboflavin, lyxoflavin was synthesized back in 1935 [2], and its optical antipode, l-lyxoflavin, was synthesized in 1949 by condensing l-lyxose with 2-amino-4,5-dimethyl-1-carboethoxyaminobenzene to give its N-glucoside, with subsequent reduction to the corresponding lyxamine, followed by hydrolysis of this compound and condensation with alloxane [1]. d-Lyxoflavin was obtained from d-lyxose through the same procedure.

It was determined in preliminary experiments that l-lyxoflavin in stimulating growth possesses a vitamin activity which differs from riboflavin activity [3]. It is possible that lyxoflavin is a special vitamin for heart muscle; it was, therefore, of interest to synthesize d- and l-lyxoflavin, and to study their biological activity.

Since the lyxoflavin molecule can be pictured as consisting of three bound parts — aromatic, aliphatic and pyrimidine — construction of the flavin molecule, therefore, can be carried out by combining the aromatic and aliphatic parts, and then with subsequent condensation of the aromatic polyhydroxyalkylamine with the pyrimidine part.

Upon condensing l-lyxose with 3,4-dimethylaminobenzene, according to the Sorokin reaction [4], by boiling in anhydrous alcohol, N-lyxofuranoside (I) was formed, which, in the presence of nickel catalyst, was converted into 3,4-xylyl-lyxamine (II), with m.p. 148-148.5°. Compared with other stereoisomeric glucamines, 3,4-xylyl-l-lyxamine possesses very low solubility in cold alcohol, and some solubility in hot alcohol. Its optical antipode resulted, with a m.p. of 150-151°, and the racemate with m.p. 131-132°.

Another nitrogen atom is introduced into the ortho-position to the existing one (which is necessary for the subsequent condensation with the pyrimidine part) of the 3,4-xylyl-lyxamine molecule (II). For this purpose, activity of the hydrogen atom in position 6 is used, which exceeds considerably the mobility of hydrogen in position 2; upon coupling of 3,4-xylyl-lyxamine with phenyldiazonium salts the azo group, therefore, enters principally at position 6, with formation of azolyxamine (III). As was demonstrated in the previous communication [5], optimal conditions for azo coupling of d-lyxamine lie in the range of pH 3-4; in this case, formation of diazoimino compound is excluded; azo coupling for the l-form was carried out by the authors.

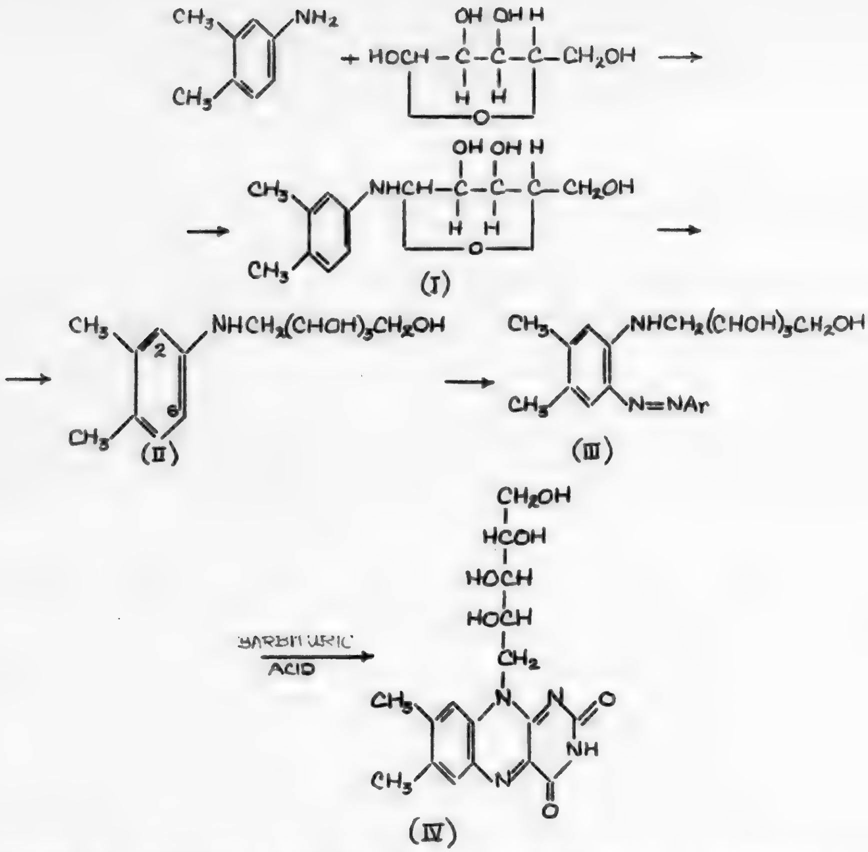
6-Phenylazo-3,4-xylyl-1-l-lyxamine (III) crystallized from 60% alcohol in the form of orange-red needles with m.p. 134-135°. Melting point of the d-form was 136.5-137.5°.

One of the proofs of structure for the azo dyes is the identity of their absorption spectra in the ultraviolet and visible ranges with the absorption spectrum for 6-phenylazo-3,4-xylyl-1-d-ribamine: I maximum 246 mμ, $\epsilon = 1.7 \cdot 10^4$; II maximum 325 m$\mu$, $\epsilon = 1.99 \cdot 10^4$; III maximum 471 m$\mu$, $\epsilon = 1.16 \cdot 10^4$. Additional proof that the azo group is in position 6 is the synthesis of corresponding lyxoflavins from azo dyes upon condensation with barbituric acid, as contrasted with the known fact that the stereoisomeric 2-phenylazo-3,4-xylyl-d-ribamine does not enter into condensation with barbituric acid [6].

For synthesis of l-lyxoflavin (IV) from the azo dye (III) and barbituric acid, as well as for synthesis of the optical antipode, N-butyl alcohol was used [7] as the medium. Purification of the flavins was carried out by reprecipitation from hydrochloric acid solutions, using hydrogen peroxide for oxidation of the reduced forms of the flavins [8].

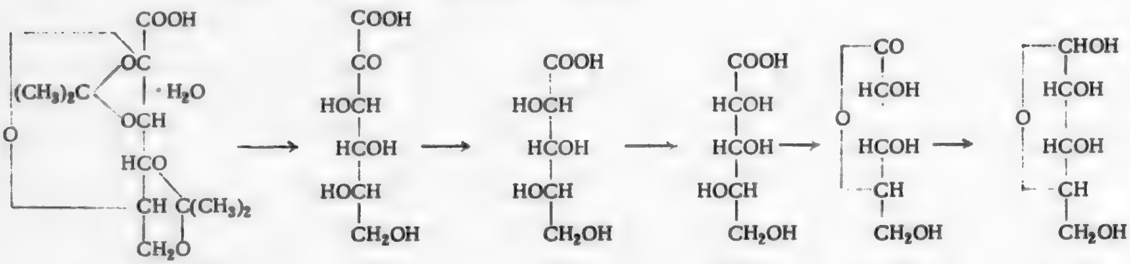
d-Lyxose, necessary for synthesis of d-lyxoflavin, was prepared by the authors according to the following scheme:

$$\text{d-galactose} \xrightarrow{\text{oxidation } Br_2 + H_2O} \text{d-galactonic acid} \xrightarrow{CaCO_3} \text{calcium d-galactonate} \xrightarrow{H_2O_2 \text{ oxidation}} \text{d-lyxose};$$



Upon oxidizing the calcium salt of galactonic acid with hydrogen peroxide in the presence of trivalent iron salts, using optimal conditions for the reaction [9], there resulted d-lyxose in 39% yield.

l-Lyxose was obtained according to the following scheme:



(V) (VI) (VII) (VIII) (IX) (X)

Diacetone-2-keto-l-gulonic acid (V) * was used as the starting product. Hydrolysis of (V) to the 2-keto-l-gulonic acid (VI), by heating its aqueous solution, took place in 76-82% yield [11]. 2-Keto-l-gulonic acid (VI), however, can be prepared directly from l-sorbose in about 50% yield by oxidation of the latter with air in sodium bicarbonate solution in the presence of platinum or palladium catalyst [12]. The oxidative rupture of 2-keto-l-gulonic acid with hydrogen peroxide into l-xylonic acid (VII) proceeds with rupture of the l-carbon, in 24% yield [13].

The authors obtained l-xylonic acid (VII) in 75% yield by direct hydrolysis of diacetone-2-keto-l-gulonic acid (V), and by oxidation with hydrogen peroxide (with 2 atoms of active oxygen). l-Xylonic acid was epimerized in the presence of organic bases to l-lyxonic acid (VIII), but not with free acid [13], although indirectly with its complex cadmium salt with cadmium bromide, an extension in this case of the procedure of epimerization of aldonic acids in the form of their salts [14]. Transition to epimeric l-lyxonic acid was 40-50%.

* Prepared from l-sorbose via diacetone-l-sorbose in 60-65% yield [10].

The $\underline{l}$-lyxono-γ-lactone (IX) was obtained from $\underline{l}$-lyxonic acid (VIII) by heating in vacuo the syrupy acid left after evaporation and removal of the cadmium ions from the cadmium salt solution. Complete elimination of bromide salts was not carried out, since their presence did not interfere with electrolytic reduction at the mercury cathode, which the authors used for conversion of $\underline{l}$-lyxono-γ-lactone (IX) into $\underline{l}$-lyxose (X).

Since the resulting $\underline{l}$-lyxose could have contained impurities of the stereoisomeric $\underline{l}$-xylose, formed because of the xylonic acid impurity present, it was, therefore, important to study the properties of the product formed from xylose, namely, 3,4-xylylxylamine, and to clarify the possibility of its purification from 3,4-xylyllyxamine. A study of the properties of 3,4-xylylxylamine was carried out with its $\underline{d}$-optical antipode. The crystalline compound failed to separate from the condensation product of $\underline{d}$-xylose with 3,4-dimethylaminobenzene after its reduction to 3,4-xylyl-$\underline{d}$-xylamine; after evaporation of the solutions, a non-crystallizing gelatinous residue remained. Upon azo coupling of this product with the phenyldiazonium salts, there was obtained 6-phenylazo-3,4-xylyl-1-$\underline{d}$-xylamine with m.p. 139.5-140° [5] (found %: N 11.81; calculated %: N 11.69) and with an absorption spectrum of: I maximum 246 mμ, II maximum 325 mμ, III maximum 471 mμ, which was identical with the absorption maxima for the stereoisomeric azoribamine. Subsequently, the authors succeeded in crystallizing 3,4-xylyl-$\underline{d}$-xylamine (upon prolonged standing) and in purifying it partially.

It was thus established that lyxamine can be readily purified from its impurity of stereoisomeric xylamine on the basis of their widely varying solubilities in water and alcohol.

While completing the present investigation, synthesis of the $\underline{l}$-form of lyxoflavin was published [15], but without isolation of the dye in the pure state; the authors started with galacturonic acid in order to obtain $\underline{l}$-lyxose.

EXPERIMENTAL

Synthesis of 3,4-Xylyl-d-xylamine

4 g of recrystallized $\underline{d}$-xylose with m.p. 149-150°, 3.2 g of 3,4-dimethylaminobenzene and 40 ml of anhydrous alcohol were heated on a water bath for 40 minutes, under reflux, to complete dissolution. The resulting N-glucoside solution was hydrogenated in a rotating autoclave over nickel catalyst at 40 atms, and a temperature of 65-70° for 2 hours. After filtration, the solvent was distilled off from solution. Syrup resulted in the residue, which, upon prolonged standing, crystallized. After washing with hot acetone, and crystallizing from a small amount of N-butyl alcohol-acetone mixture (2:3), there resulted 3,4-xylyl-$\underline{d}$-xylamine in the form of colorless clusters of thin needles with m.p. 129-130°. The product was very soluble in ethyl alcohol and water.

6.100 mg sub.: 0.270 ml N_2 (19°, 548 mm). Found %: N 5.08. $C_{13}H_{21}O_4N$. Calculated %: N 5.48.

Synthesis of d-Lyxoflavin

Calcium d-galactonate. 120 g of $\underline{d}$-galactose was dissolved in 500 ml of water, 45 ml of bromine added, and after complete dissolution of bromine, it was left to stand for 48 hours in darkness. Bromine excess was then removed from the warm solution by air-blowing, 90 ml of 40% sodium hydroxide added, and then 40 g of chalk; after heating on a boiling water bath for 1.5 hours, the mixture was filtered. After cooling, crystallization began; the precipitate was filtered and washed with 30% alcohol. 117 g of calcium galactonate resulted, and then after evaporation of the solution twice, another 18 g resulted; yield was 77.7%.

d-Lyxose. 80 g of calcium $\underline{d}$-galactonate was dissolved in 1,000 ml of hot distilled water, and it was then mixed with a solution of 1.4 g of ferric sulfate [$Fe_2(SO_4)_3 \cdot 9H_2O$] in 12 ml of water, and 2 g of barium acetate in 12 ml of water. 80 ml of 30% hydrogen peroxide diluted with 200 ml of water was added uniformly to the mixture at 60° over a period of 1.5 hours. Several minutes following start of addition of hydrogen peroxide, evolution of carbon dioxide. After a half-hour addition of the total quantity of hydrogen peroxide, and cessation of the gas evolution, the mixture was filtered, and the solution evaporated in vacuo to a volume of 80 ml at a bath temperature of not over 60°. 480 ml of methyl alcohol was added to the residue with stirring, and then 320 ml of acetone at room temperature. After 5 minutes, the resulting precipitate was filtered off, washed with methyl alcohol, and the filtrate evaporated in vacuo to the consistency of syrup. 26.6 g of syrup resulted, with a content of 62.8% lyxose; yield was 39%.

3,4-Xylidine-N-d-lyxofuranoside. A mixture of 4 g of $\underline{d}$-lyxose, 3.2 g of 3,4-dimethylaminobenzene and 60 ml of anhydrous alcohol was heated with reflux condenser on a water bath for 15-20 minutes to complete dissolution. A crystalline precipitate separated, which was filtered off and washed with alcohol. 5.75 g (85%) of 3,4-xylidine-N-$\underline{d}$-lyxofuranoside in the form of colorless platelets resulted, with m.p. 146-147°.

3.040 mg sub.: 6.840 mg CO_2; 1.935 mg H_2O. 3.915 mg sub.: 0.147 ml N_2 (24°, 746 mm). Found %: C 61.35; H 7.10; N 5.02. $C_{13}H_{19}O_4N$. Calculated %: C 61.64 H 7.56; N 5.53.

3,4-Xylyl-d-lyxamine. 3.3 g of the prepared N-glucoside and 70 ml of anhydrous alcohol were hydrogenated in a rotating autoclave in the presence of nickel catalyst under a pressure of 40 atms and 65-70° for 2 hours. After decanting off the hot alcoholic solution from the catalyst, and cooling, a compound separated which was recrystallized from water. 2.5 g (74%) of 3,4-xylyl-d-lyxamine resulted in the form of lustrous needles.

M.p. 150-151°, $[\alpha]_D^{18}$ + 31.5° (concentration of 5% in 2 N HCl).

5.411 mg sub.: 0.263 ml N_2 (22°, 745 mm). Found %: N 5.51. $C_{13}H_{21}O_4N$. Calculated %: N 5.48.

6-Phenylazo-3,4-xylyl-1-d-lyxamine. 1 g of lyxamine was dissolved in 100 ml of hot water, 0.5 ml of pure hydrochloric acid added, and carefully, to avoid crystallizing, cooled to 20-25°. The lyxamine solution was added with stirring to a diazonium salt solution prepared from 0.46 g of aniline, 0.66 g of sulfuric acid and 0.34 g of sodium nitrite. The azo coupling was carried out at 18-20° and at a pH of 3.8-4.0, attained by addition of 15% sodium acetate solution, and then maintained so for the 3-hour period. The resulting precipitate was filtered off, washed with water, and dried in air. 1.14 g (80.8%) of the azo dye was obtained, with a m.p. of 105-110°. The crude compound dissolved very readily in organic solvents — alcohols, benzene, chloroform, acetone and others. To purify it, the substance was dissolved in alcohol, filtered from impurities, and left for slow crystallization with the solvent evaporated almost to dryness. The residue was washed on a filter with 50% alcohol, and recrystallized several times from a small amount of 50-60% alcohol. 6-Phenylazo-3,4-xylyl-1-d-lyxamine resulted in the form of long needle clusters, red in color, with m.p. 136-136.5°, or with rapid crystallization, in the form of separate, thin needles, orange-red in color, with m.p. 136.5-137.5°.

4.593 mg sub.: 0.462 ml N_2 (22°, 746 mm). Found %: N 11.43. $C_{19}H_{25}O_4N_3$. Calculated %: N 11.69.

d(+)-Lyxoflavin. A mixture of 0.5 g of azolyxamine, 0.3 g of barbituric acid, 6 ml of n-butyl alcohol and 1 ml of glacial acetic acid was heated with reflux condenser on a boiling water bath for 5 hours with stirring. There gradually accumulated on the wall of the flask a dark-yellow precipitate, which, after termination of reaction, was filtered off, washed with butyl alcohol, and then with boiling water. 0.25 g of crude d-lyxoflavin resulted. It was dissolved in 1 ml of pure hydrochloric acid, and after complete dissolution 1 ml of water and 2 drops of hydrogen peroxide were added. The solution was filtered and poured into 6 ml of hot water. The resulting precipitate was stirred in the hot state for several hours. d-Lyxoflavin was obtained in the form of yellow needles with m.p. 276-278° (with decomposition).

$[\alpha]_D^{20}$ + 46° ± 5° (concentration 0.25% in 0.05 N NaOH). The absorption spectrum possessed maxima at 445, 370, 265 and 222 mμ. Found %: N 14.43, 14.44. $C_{17}H_{20}O_6N_4$. Calculated %: N 14.90.

Synthesis of 1-Lyxoflavin

1-Xylonate cadmium-cadmium bromide $[(C_5H_9O_6)_2Cd \cdot CdBr_2 \cdot 2H_2O]$. 200 g of diacetone-2-keto-1-gulonic acid (hydrated) (V) was dissolved in 600 ml of distilled, boiling water and for the hydrolysis, was boiled for 40 minutes. The solution was then neutralized with 40 g of sodium carbonate and oxidized at 0° by adding 160 ml of 30% perhydrol for 1 hour. After completion of the oxidation, the solution was acidified with hydrochloric acid (d 1.19) and evaporated to a syrup in vacuo. The residue was diluted with 300 ml of water and treated with 65 g of cadmium carbonate, heating to boiling. After cessation of the foaming, the excess cadmium carbonate was filtered off and the filtrate poured into a solution of aqueous cadmium bromide. After cooling, crystallization started. The precipitate was filtered off on the following day and washed with ice water. 192 g (75%) of the double cadmium salt of 1-xylonate resulted.

Found %: Cd 29.73. $C_{10}H_{18}O_{12}Br_2Cd_2 \cdot 2H_2O$. Calculated %: Cd 29.95.

1-Lyxono-γ-lactone (IX). 1-Xylonic acid (VII) was epimerized directly into 1-lyxonic acid (VIII), the former being in the form of the double salt, 1-xylonate cadmium-cadmium bromide, from which resulted 1-lyxono-γ-lactone upon treating the cadmium salt with hydrogen sulfide, following by heating of the evaporated residue in vacuo.

40 g of the double salt, 500 ml of water and 50 ml of pyridine were placed in a rotating autoclave; epimerization was carried out for 5 hours at a temperature of 144-146°, air being displaced by nitrogen. A mixture consisting of the solution and the complex compound of cadmium bromide with pyridine ($CdBr_2 \cdot C_5H_5N$), was removed, and the pyridine distilled out with steam; thereupon, the precipitate gradually went into solution. The solution was filtered while hot and the filtrate evaporated in vacuo to 50 ml, whereupon a crystalline precipitate of the double salt separated; it was filtered off after cooling. The xylonate cadmium-cadmium bromide recovered from the reaction was about 15-20 g. After dilution of the filtrate with 100 ml of water, the cadmium was precipitated with hydrogen sulfide. The cadmium sulfide precipitate was filtered off, the solution of 1-lyxonic acid clarified with

activated charcoal and heat, and after filtration, it was evaporated in vacuo to 50 ml. The residue was neutralized with sodium hydroxide to a pH of 2.5, and after filtration, and second clarification, using activated charcoal, it was evaporated to a syrup in vacuo, which was kept on a boiling water bath in vacuo for 2 hours. 36 g (65%) of crude l-lyxono-γ-lactone was obtained from 140 g of xylonate which entered into reaction (from several experiments).

l-Lyxose (X). l-Lyxono-γ-lactone was converted into l-lyxose by electrical reduction on a mercury cathode. An electrolyzer with membrane was used. 10% sulfuric acid served as anolyte, lead being used for the anode. The catholyte contained 10% lactone and 10% sodium sulfate. Electrolysis was carried out at 13-15°, and 5-6 V. Stirring was continued for the duration of electrolysis, and the pH kept at a level of 3.5-4.5. After termination of reduction, l-lyxose solution containing sodium sulfate and aldonic acid salts was evaporated in vacuo (bath temperature 50°) to 70 ml volume.

350 ml of methyl alcohol was added to the residue, and the sodium sulfate which separated was filtered off and washed with methyl alcohol. The filtrate was evaporated in vacuo to 60 ml, diluted with water to 180 ml, and treated with excess barium carbonate, and stirring, on a boiling water bath for 30 minutes. After filtration, the solution was evaporated in vacuo to a thin syrup, which was again treated with methyl alcohol, with stirring. The precipitate which separated was filtered off and the solution again evaporated to a syrup. 15 g of syrup, with 6 g of l-lyxose content, resulted.

3,4-Xylyl-l-lyxamine (II). 5 g of l-lyxose and 4 g of 3,4-dimethylaminobenzene in 60 ml of anhydrous alcohol was condensed to 3,4-xylidine-N-l-lyxofuranoside (I), by heating on reflux and a water bath for 30 minutes. The N-glucoside solution which resulted was hydrogenated in a rotating autoclave with nickel catalyst at 70° and 40 atms for 2 hours. The hot solution was decanted from the catalyst and then filtered. The resulting precipitate was recrystallized from water. 3.6 g (42%) of 3,4-xylyl-l-lyxamine in the form of colorless needles with m.p. 148-148.5° resulted (m.p. 147-148° according to the literature data [15]).

$[\alpha]_D^{20}$ −32.5° (concentration 2% in 2 N HCl). Found %: N 5.55. $C_{13}H_{21}O_4N$. Calculated %: N 5.48.

3,4-Xylyl-dl-lyxamine. Obtained by mixing solutions of optical antipodes in the form of needles with m.p. 131-132° (from alcohol). Recrystallization did not increase the melting point.

6-Phenylazo-3,4-xylyl-1-l-lyxamine (III). Prepared from lyxamine (II) by the same procedure as for its optical antipode. The azo dye crystallized from aqueous alcohol in the form of red needles with m.p. 134-135°.

3.686 mg sub.: 0.382 ml N_2 (19°, 741 mm). Found %: N 11.79. $C_{19}H_{25}O_4N_3$. Calculated %: N 11.69.

l-Lyxoflavin (IV). Prepared from azolyxamine (III) and barbituric acid in the presence of acetic acid in n-butyl alcohol medium by the same procedure as was described for its optical antipode. l-Lyxoflavin was in the form of yellow needles with m.p. 277-279°.

$[\alpha]_D^{20}$ −45° ± 5° (concentration 0.4% in 0.05 N NaOH).

Its absorption spectrum, from the extinction values and from the maxima (λ = 445, 370, 265 and 222 mμ) was identical to the absorption spectra for d-lyxoflavin and d-riboflavin.

Found %: N 14.32. $C_{17}H_{20}O_6N_4$. Calculated %: N 14.90.

SUMMARY

1. Synthesis of l-lyxose from diacetone-2-keto-l-gulonic acid by a series of conversions has been attained. Epimerization of l-xylonic acid has been carried out in the form of its double cadmium salt. l-Lyxonic acid has been converted into l-lyxose by lactonization and electrolytical reduction on a mercury cathode.

2. d- and l-lyxoflavins have been synthesized by condensing lyxose with 3,4-dimethylaminobenzene, reduction of the resulting N-glucoside to lyxamine, its azo coupling, and condensation of the azo dye with barbituric acid.

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INVESTIGATIONS IN THE FIELD OF TAUTOMERIC COMPOUNDS

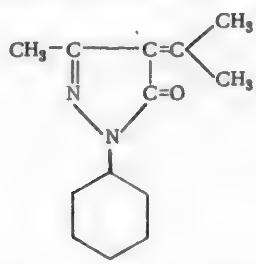
XV. INTERACTION OF PHENYLMETHYLPYRAZOLONE WITH KETONES

A. E. Porai-Koshits* and M. S. Dinaburg

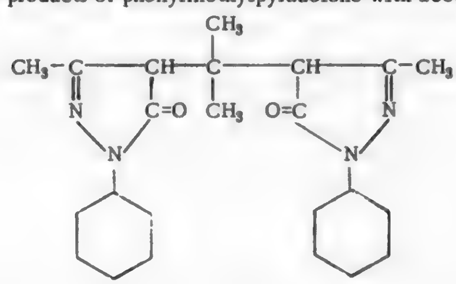
As one of the authors has demonstrated with N. V. Khromov [1], the condensation products for a number of iso-oxazolone derivatives with ketones, of the type $R{=}C\langle{}^{CH_3}_{R'}$, where R is the isooxazolone radical, and R' equals CH_3, or aryl, possess high mobility of the hydrogen atoms in the methyl groups. This mobility is evidenced in their ability to enter into reaction with aldehydes and diazo- and nitro- compounds, which lead to new compounds of interest from both a theoretical and a practical viewpoint. Condensation products of phenylmethylpyrazolone with ketones, constructed according to the type indicated (where R = the phenylmethylpyrazolone radical, and R' is CH_3 or aryl) should also possess analogous properties.

Because of the fact that literature data on synthesis of similar-type compounds are very meager, and are for the most part limited to an early work by Knorr [2], the authors considered it necessary to carry out a thorough research on their properties and methods of synthesis.

As is known, Knorr obtained condensation products of phenylmethylpyrazolone with acetone (I) and (II):



(I)



(II)

The structures of these compounds have subsequently been quite convincingly proved [3, 4]; a thorough study of their chemical properties and conversions, however, was not carried out.

Early investigation of the synthesis of substance (I) brought to light the fact that it always resulted in a mixture with (II), the amount of latter depended upon the excess of acetone taken, and rapidly increased (compound II) when acetone was in slight excess. At the same time, large acetone excess had very little effect upon increasing the yield of (I). Isopropylidenephenylmethylpyrazolone (I) converted with great ease into the compound (II) when reacted with phenylmethylpyrazolone in alcoholic solution, or by direct melting of the initial compounds.

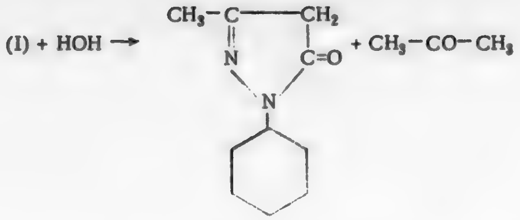
Conversion of compound (II) into (I), when reacted with acetone, did not occur, as might be expected according to the scheme

$$(II) + CH_3{-}CO{-}CH_3 \rightarrow 2\,(I),$$

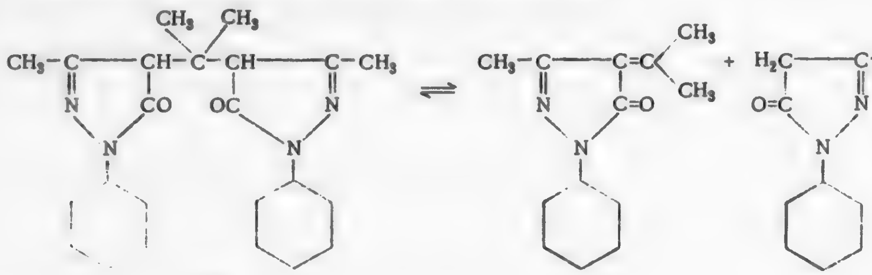
because of which fact accumulation of compound (II) occurred in the reaction mass.

Isopropylidenephenylmethylpyrazolone (I) is noted by its instability, especially when reacted with compounds of basic nature. Even upon short heating in alcohol, containing traces of alkali hydroxide, sodium carbonate or sodium acetate, it converted almost completely into (II), apparently as a result of reaction

* Deceased.



with subsequent interaction of the initial product with the phenylmethylpyrazolone formed. On the other hand, compound (II) is stable to the action of bases and caustic alkali. Its solutions in alkalies can be stored for a long time without noticeable decomposition. When boiled in alcohol, however, it decomposed partially into phenylmethylpyrazolone and isopropylidenephenylmethylpyrazolone; the latter could be isolated by rapid cooling of the solution. They both interacted with each other, and only the product (II) separated on gradual cooling of the alcoholic solution. Consequently, there existed an equilibrium in the solution:

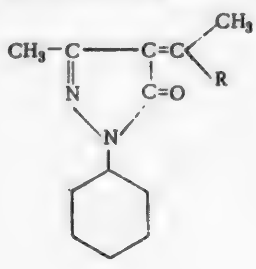


(II) (I)

Upon heating the compound (II) in glacial acetic acid, or above its melting point, the equilibrium was shifted to the right (see experimental); therefore, by carrying out condensation of phenylmethylpyrazolone with an equimolecular amount of acetone in glacial acetic acid at 140° (in a sealed tube), it was possible to obtain up to 70-75% of compound (I). Nevertheless, even under these conditions, a certain amount of the product (II) resulted, chiefly by cooling the tubes. Lowering the reaction temperature to 100-110°, or by slow cooling of the tubes in an oven, the yield of compound (I) was decreased to 35-40%.

It could have been expected that the above-described properties for condensation products of phenylmethylpyrazolone with acetone would also be characteristic for other representatives of this group. To verify this assumption, the reactions of phenylmethylpyrazolone with acetophenone and m-nitroacetophenone were studied.

Acetophenone and m-nitroacetophenone entered into reaction with phenylmethylpyrazolone, forming derivatives not described in the literature, whose structure and properties correspond to the formula (III):



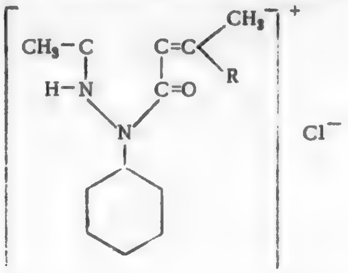
(III)

where R = C_6H_5 or m-$C_6H_4NO_2$.

It is characteristic that in this case no products similar to compound (II) were formed according to our observations. In contrast to the acetone analog these compounds did not enter into reaction with phenylmethylpyrazolone, and a product similar to compound (II) failed to form, even when using a very large excess of phenylmethylpyrazolone, and under a large variety of conditions for the reaction course.

Acetone, acetophenone and m-nitroacetophenone derivatives constructed according to type (I), displayed clearly amphoteric properties.

Thus, on the one hand, they are all capable of adding hydrogen chloride, apparently thanks to the imino nitrogen of the pyrazolone ring, forming salts, the structure of which can be represented by the formula:



These salts are very unstable and in the air lose hydrogen chloride immediately, converting into the initial bases. They can be kept for a long time in crystalline form in anhydrous ether with hydrogen chloride. On the other hand, they are soluble in alkali. While isopropylidenephenylmethylpyrazolone dissolves in alcoholic alkali and disintegrates rapidly, acetophenone and m-nitroacetophenone derivatives form stable alkaline solutions, from which they can be isolated by acidification. The latter of these products possess such a well-defined acid character, that it dissolved even in dilute aqueous alkali.

EXPERIMENTAL

Condensation of phenylmethylpyrazolone with acetone, according to Knorr. 17.4 g (0.1 mole) of phenylmethylpyrazolone and 57 g (1.0 mole) of acetone were heated under reflux on a water bath for 6 hours. After 12 hours, the resulting precipitate was filtered off and washed with acetone, dilute alkali, water, and dried in a desiccator. The yield was 9.5 g, m.p. 114-115°, Bright-yellow, lustrous crystals from alcohol, m.p. 116-117°. The white crystalline product separated upon acidification of the alkaline filtrate with dilute HCl. Yield was 1.35 g. White prisms from alcohol, with m.p. 138°. The acetone mother liquor was diluted with water, the resulting precipitate treated as with the basic precipitate. Yield of the yellow compound was 0.87 g, m.p. 104-109°; white, 8.10 g, m.p. 129-130°. The total yield of yellow compound was 10.37 g (46.8%), and of white, 9.45 g (48.7%). The properties of these compounds coincided with those indicated in the literature [2, 3, 4].

The effect of acetone excess upon the ratio of yield of white and yellow products is given in the table.

TABLE

Moles taken for reaction		Mole ratio	Yield (%)	
phenylmethylpyrazolone	acetone		compound (I)	compound (II)
0.02	0.01	0.5	–	96.0
0.02	0.05	2.5	5.6	87.8
0.02	0.1	5	29.5	68.5
0.02	0.2	10	47.0	48.7
0.02	0.4	20	51.0	46.4
0.02	1.0	50	46.9	46.6

Condensation of isopropylidenephenylmethylpyrazolone with phenylmethylpyrazolone. a) 2.14 g (0.01 mole) of compound (I), 1.75 g of phenylmethylpyrazolone, and 10 ml of methyl alcohol were heated under reflux. After 30 minutes, white crystals began to separate. After 12 hours, the precipitate was filtered and washed with ether. White lustrous prisms (from alcohol), m.p. 138°. Yield was 3.8 g (96%). There was no depression in melting point of the mixture when mixed with the white compound prepared according to the method of Knorr.

b) 2.14 g of the substance (I) and 1.75 g of phenylmethylpyrazolone were mixed thoroughly in a reaction flask at 100°. The yellow melt which formed at the beginning soon solidified to a solid white mass. Heating was continued for 3 hours, and then the melt was powdered in a mortar, and washed with ether. The yield of white product was 3.07 g (77.5%). From alcohol – white crystals with m.p. 138°.

Rupture of the white compound. 1.94 g of the white compound (m.p. 138°) was heated with 10 ml of ethyl alcohol for 30 minutes. The solution was cooled rapidly with salt-ice mixture. A bright-yellow crystalline precipitate separated immediately. The yield was 0.4 g. Bright-yellow needles with m.p. 117° from glacial acetic acid. A small amount of white crystals with m.p. 136-137° precipitated from the alcoholic mother liquor upon standing, after separation of the yellow crystals. After their separation, the filtrate was heated to boiling and diluted with 15 ml of water. The remaining white compound separated in the form of an oil. Phenylmethylpyrazolone (m.p. 122-124°) precipitated in the form of long, white needles from the water-alcoholic solution upon cooling. Only the white compound precipitated upon slow cooling of the alcoholic solution.

Synthesis of isopropylidenephenylmethylpyrazolone in glacial acetic acid. 17.4 g of phenylmethylpyrazolone, 15 ml of acetone (13.0 g) and 15 ml of glacial acetic acid were heated in a sealed tube at 140° for 6 hours. The tube was cooled as rapidly as possible to 40-50° and opened; the tube contents were transferred to a beaker, where it crystallized immediately. The yield was 15.2 g (71.0%), m.p. 115-116°. From acetic acid – needles with m.p. 117°. If the tube is cooled slowly, the yield falls to 44% and below.

Rupture of isopropylidenephenylmethylpyrazolone (I). 2.14 g of the substance (I) was heated with 10 ml of 95% alcohol. 2 drops of 0.5% sodium hydroxide solution was added to the hot solution. The solution turned to a red-brown color and after 2-3 minutes, fine, white prisms began to crystallize. White prisms with m.p. 138° from alcohol.

Attempt to convert the compound (II) into (I). a) 3.0 g of the compound (II) was boiled with 15 ml of acetone under reflux for 2 hours. The precipitate gradually went into solution and separated upon cooling. White prisms with m.p. 136°. A similar result was obtained upon heating for 10, 15 and 30 hours.

b) 3.0 g of compound (II) and 30 ml of acetone were heated in a sealed tube at 120° for 2 hours. The initial compound reprecipitated.

Condensation of phenylmethylpyrazolone with acetophenone (4-α-phenylethylidenephenylmethylpyrazolone). 17.4 g (0.1 mole) of phenylmethylpyrazolone and 12.0 g (0.1 mole) of acetophenone in a flask equipped with air condenser were heated in an oil bath at 100°, everything passing into solution, and at 145° an intense evolution of water beginning. After 3 hours, the mass was transferred to a beaker and stirred vigorously with a rod to the start of crystallization; after 1.5-2.5 hours, the mass solidified. After 12 hours, it was ground in a mortar with 100 ml of gasoline (b.p. 70-90°), separated, washed on a filter with 100-150 ml of gasoline and 25-30 ml of methyl alcohol; afterwards, it was washed in a beaker with dilute alkali solution (~ 5 - 10 %), water and dilute acetic acid. Yellow prisms with m.p. 88-89° from ethyl alcohol. Yield of pure product 17.9 g (65%). Soluble in alcohol, acetone, ether, glacial acetic acid. Insoluble in ligroin and petroleum ether.

0.1506 g sub.: 13.2 ml N_2 (21°, 776 mm). 0.0840 g sub.: 7.3 ml N_2 (21°, 780 mm). 0.1740 g sub.: 0.4985 g CO_2; 0.0985 g H_2O. 0.1518 g sub.: 0.4361 g CO_2; 0.0820 g H_2O. Found %: C 78.27, 78.32; H 6.20, 6.01; N 10.34, 10.30. $C_{18}H_{16}ON_2$. Calculated %: C 78.26; H 5.79; N 10.14.

Condensation of phenylmethylpyrazolone with m-nitroacetophenone (3-nitrophenyl-4-α-ethylidenephenylmethylpyrazolone). 7.0 g of phenylmethylpyrazolone and 6.6 g of m-nitroacetophenone were placed in a flask equipped with reflux condenser in an oil bath heated at 150°. Reaction began immediately, as noted by the evolution of water. The melt was cooled and ground thoroughly with 10 ml of glacial acetic acid. After a given time, all the mass had crystallized. The precipitate was filtered off, washed with a small amount of acetic acid, and then with ether. Yield was 4.5-5.0 g (35-40%). The compound was soluble in toluene, xylene, glacial acetic acid, poorly so in benzene, very poorly so in ethyl and methyl alcohols and acetone, and insoluble in ether. Yellow prisms from 85% acetic acid, with m.p. 150-151°.

0.1004 g sub.: 11.4 ml N_2 (22°, 762 mm). 0.1029 g sub.: 0.2541 g CO_2; 0.0456 g H_2O. Found %: C 67.39; H 4.96; N 13.17. $C_{18}H_{15}O_3N_3$. Calculated %: C 67.29; H 4.98; N 13.08.

Attempt at condensation of 4-α-phenylethylidene- and 3'-nitrophenyl-4-α-ethylidenephenylmethylpyrazolones with phenylmethylpyrazolone. Attempts to effect this reaction, carrying out at various temperatures and duration times for the experiments, heating in solvents, or melting, with various amounts of initial compounds and various temperatures, were of no avail. In all cases, the reaction mass converted into the original compounds.

Reaction of alkali with 4-α-phenylethylidenephenylmethylpyrazolone. 2.76 g of the compound was dissolved in 15 ml of ethyl alcohol and 5 ml of 20% sodium hydroxide added to the solution. The orange-red solution did not change color on boiling. The solution was diluted with water to 250 ml and acidified with dilute hydrochloric acid. The resulting precipitate was filtered off, washed with water, and recrystallized from ethyl alcohol. Yellow crystals with m.p. 87-88°. Boiling the alkaline solution for 5 hours produced decomposition of the compound and a pronounced odor of acetophenone was apparent.

Alkaline reaction with 3'-nitrophenyl-4-α-ethylidenephenylmethylpyrazolone. 0.3 g of the compound was dissolved, in the cold, in 50 ml of 0.1 N sodium hydroxide solution. From the yellowish solution, the initial product was isolated in the form of a yellowish, flaky precipitate by means of carbon dioxide.

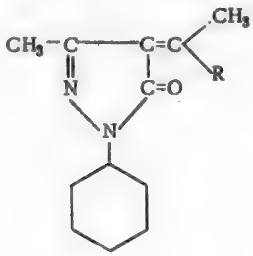
Reaction of dry hydrogen chloride with 4-isopropylidene-4-α-phenylethylidene- and 3'-nitrophenyl-4-α-ethylidenephenylmethylpyrazolone. 2.14 g of 4-isopropylidenephenylmethylpyrazolone was dissolved in 25 ml of anhydrous ether and dry hydrogen chloride passed into the solution. Separation of a colorless oil began immediately, which, when rubbed with a rod, solidified to a colorless, crystalline mass. The crystals were stable in

saturated hydrogen chloride, and when separated from the liquid, they immediately melted to a brown resinous mass, which crystallized with difficulty.

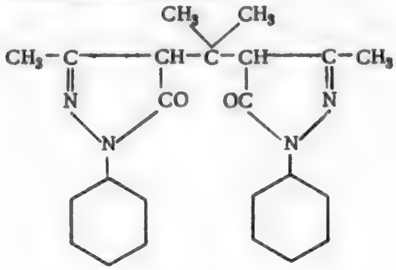
4-α-Phenylethylidene- and 3'-nitrophenyl-4-α-ethylidenephenylmethylpyrazolone behave similarly, with the difference that the oil separating upon decomposition of the hydrochloride crystallizes more readily.

SUMMARY

1. Acetone, acetophenone and its derivatives substituted in the ring, enter into reaction with one or two molecules of phenylmethylpyrazolone, forming a compound of the type:



or



(I) (II)

where R equals aromatic or aliphatic radical.

2. The dominant direction of the reaction depends upon the nature of reacting ketone. Thus, with acetone, approximately equal amounts of compounds (I) and (II) are formed, while acetophenone and m-nitroacetophenone produce only interaction products with one molecule of phenylmethylpyrazolone.

3. The formation of a mixture of compounds in the case of phenylmethylpyrazolone interaction with acetone is explainable by the ability of a compound of type (I) formed, to react in turn with phenylmethylpyrazolone, forming compound (II).

4. Compounds of type (I) possess definite amphoteric properties.

LITERATURE CITED

[1] A. E. Porai-Koshits and N. V. Khromov, J. Gen. Chem., 10, 1829 (1947).

[2] Knorr, Ann., 238, 179 (1887).

[3] Pauly, Ber., 30, 484 (1897).

[4] Stolle, Ber., 38, 3028 (1905).

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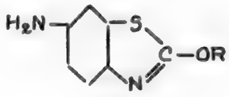
2-ALKOXYMETHYL- AND 2-ARYLOXYMETHYL-6-AMINOBENZTHIAZOLES

S. G. Fridman

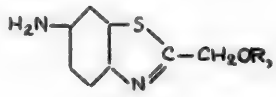
Alkoxyamino derivatives of heterocyclic nitrogen compounds — pyridine, quinoline, benzthiazole — attracted long ago the attention of investigators because of their high bacteriostatic action upon the tuberculosis bacillus [1].

The synthesis of 2-alkoxy- and 2-aryloxy-6-aminobenzthiazoles (I) was described in the author's preceding work [2].

The task of the present work was a synthesis of methylene homologs of the preparations obtained earlier, namely: 2-alkoxymethyl and 2-aryloxymethyl-6-aminobenzthiazoles (II):



(I)

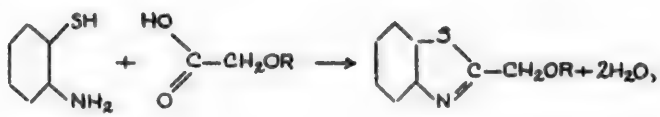


(II)

where R = alkyl, aryl or aralkyl.

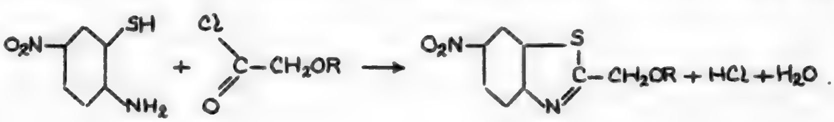
Synthesis of this type of compound can be attained in two ways.

I. Obtaining 2-alkoxymethylbenzthiazoles by condensation of o-aminophenylmercaptan with alkoxyacetic acids



and then nitrating the resulting bases.

II. Obtaining 2-alkoxymethyl- and 2-aryloxymethyl-6-nitrobenzthiazoles by condensation of 5-nitro-2-aminophenylmercaptan with the chloroanhydrides of alkoxy and aryloxyacetic acids according to the equation



The reduction of 6-nitro derivatives obtained by either method was expected to produce amines of interest to the author.

The initial materials required, namely aryloxyacetic acids, are described in the literature.

Constants, found by the author and found in the literature for alkoxy- and aryloxyacetic acids, which were used in the present work, are given in Table 1.

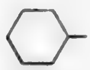
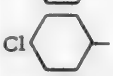
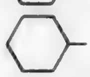
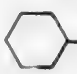
Condensation of o-aminophenylmercaptan with alkoxyacetic acid was carried out by heating the components at 135-140° for 3-4 hours. The 2-alkoxymethylbenzthiazoles synthesized by the author, are given in Table 2.

Preparations I and II given in Table 2 were synthesized by the same procedure as by other authors [14, 15]. V. M. Zubarovsky synthesized preparations III, V and IX by interacting 2-bromomethylbenzthiazole with the corresponding alcoholates [16].

2-Alkoxymethylbenzthiazoles are colorless liquids, with the exception of 2-isopropoxymethylbenzthiazole (IV), which had a m.p. of 39°, and 2-cyclohexyloxymethylbenzthiazole (VIII) with a m.p. of 59°.

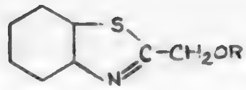
TABLE 1

Alkoxy- and Aryloxyacetic Acids of the General Formula $ROCH_2COOH$

Preparation Number	R	Boiling point: author's data	Boiling point: literature data	Melting point: author's data	Melting point: literature data	Yield (%)	Literature
I	CH_3-	197-198°	99-100° (25 mm)	–	–	53	[3]
II	CH_3CH_2-	97 (7 mm)	109-111 (17-18 mm)	–	–	70	[4]
III	$CH_3CH_2CH_2-$	110-112 (12 mm)	108 (10 mm)	–	–	61	[5]
IV	$(CH_3)_2CH-$	97-101 (5 mm)	113 (21 mm)	–	–	49	[3]
V	$CH_3CH_2CH_2CH_2-$	115-117 (11 mm)	115-116 (10 mm)	–	–	72	[5]
VI	$(CH_3)_2CHCH_2-$	107-108 (11 mm)	118 (18 mm)	–	–	87	[3]
VII	$(CH_3)_2CHCH_2CH_2-$	235; 117-119 (5 mm)	235	–	–	83	[6]
VIII	$n-C_8H_{17}-$	163-166 (11 mm)	125-126 (12 mm)	–	–	63	[5]
IX	$CH_2(CH_2-CH_2)_2CH-$ (cyclohexyl)	155-159 (20 mm)	165 (25 mm)	–	–	61	[7]
X	$CH_2=CH-CH_2-$	118-120 (10 mm)	120 (13 mm)	–	–	59	[8]
XI		–	–	99	99°	54	[9]
XII	Cl 	–	–	154-155	155-156	78	[10]
XIII	Br 	–	–	160-161	161-162	51	[11]
XIV	CH_3O 	–	–	111-112	110-112	49	[11]
XV	 OCH_3	–	–	122-123	121	65	[12]
XVI	 CH_2-	165 (5 mm)	136 (0.2 mm)	–	–	68	[13]

The reaction of nitric acid with alkoxyderivatives of heterocyclic nitrogen compounds has received but little study. It is known that upon nitrating benzyl alcohol esters, the nitro group moves chiefly to the p-position [17]. Isobutyl- and isoamyl-benzyl esters react with nitric acid (d 1.5) to form benzaldehyde and the corresponding alkylnitrates [18].

TABLE 2

2-Alkoxymethylbenzthiazoles of the General Formula 

Preparation Number	R	Boiling point	Yield (%)	Empirical formula	Analytical results			
					nitrogen (%)		sulfur (%)	
					found	calc'd	found	calc'd
I	CH_3-	135-138° (5 mm)	68	–	–	–	–	–
II	CH_3CH_2-	141-142 (7 mm)	58	–	–	–	–	–
III	$CH_3CH_2CH_2-$	151-152 (7 mm)	49	$C_{11}H_{13}ONS$	6.79 6.84	6.76	15.45 15.30	15.46
IV	CH_3 $>CH-$ . . . . CH_3	150-152 (10 mm) M.p. 39°	60	$C_{11}H_{13}ONS$	6.69 6.52	6.76	15.30 15.40	15.46
V	$CH_3CH_2CH_2CH_2-$	163-164 (6 mm)	67	$C_{12}H_{15}ONS$	6.06 6.11	6.33	13.97 14.28	14.48
VI	CH_3 $>CHCH_2-$ . . . . CH_3	133-134 (3 mm)	72	$C_{12}H_{15}ONS$	6.18 6.28	6.33	14.25 14.15	14.48
VII	CH_3 $>CHCH_2CH_2-$ . . . . CH_3	151-152 (3 mm)	69	$C_{13}H_{17}ONS$	5.95 5.89	5.95	13.70 13.66	13.61
VIII	CH_2-CH_2 CH_2 $CH-$ . . . . . CH_2-CH_2	183-186 (7 mm) M.p. 59°	57	$C_{14}H_{17}ONS$	5.70 5.72	5.66	12.78 12.73	12.95
IX	$CH_2=CH-CH_2-$	151-152 (7 mm)	51	$C_{11}H_{11}ONS$	6.91 6.96	6.82	15.49 15.75	15.60

Under these conditions, p-tolylbenzylic ester forms benzaldehyde, 3,5-dinitro-4-oxy-methylbenzene and 4-nitrobenzyl nitrate [19]. The dibenzyl ester does not give a nitration product, but only the oxidation products, namely, benzaldehyde and benzoic acid [17].

Nitration of 2-alkoxymethylbenzthiazole was carried out in the author's work. Reacting the nitration mixture with 2-methoxymethyl- (I), 2-ethoxymethyl- (II), 2-propoxymethyl- (III) and 2-butoxymethyl- (V) -benzthiazoles, gave products in the molecules of which the nitro group occupied the 6 position. This fact was proved by oxidation of the resulting nitro derivatives to nitrobenzthiazole-2-carboxylic acid, and its decarboxylation to 6-nitrobenzthiazole.

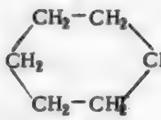
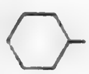
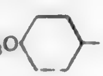
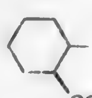
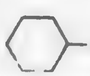
Nitration of 2-isopropoxymethyl-(IV), 2-isobutoxymethyl-(VI), 2-isoamyloxymethyl-(VII) and 2-allyloxymethyl-(IX)-benzthiazoles under the same conditions leads to formation of 2-oxymethyl-6-nitrobenzthiazole. Thus, along with the nitration process, there occurs desalkylation of the alkoxy group containing the branched chain of carbon atoms, or the multiple bond.

Similar weakening of stability in the branched alkyl bond with ester oxygen was observed by Tronov and Ladygina [20], during hydrolysis of the alkyl esters of phenol with hydrobromic acid.

Upon nitration of the indicated 2-alkoxymethylbenzthiazoles, containing branched alkyl or allyl radicals, 2-benzthiazolylaldehyde was isolated from acetic anhydride medium, i.e., under these conditions, nitration does not proceed at all, but oxidation of the alkoxymethyl group to the aldehyde group occurs. As was indicated above, a similar phenomenon is observed upon nitrating isobutyl- and isoamylbenzyl esters, as well as by nitrating the dibenzyl ester.

TABLE 3

Chloroanhydrides of Alkoxy- and Aryloxyacetic Acids of the General Formula $ROCH_2COCl$

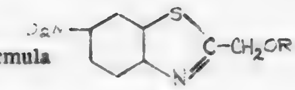
Preparation Number	R	Boiling point: author's data	Boiling point: literature data	Yield (%)	Literature
I	$(CH_3)_2CH-$	127-129°	139-141°	87	[21]
II	$(CH_3)_2CHCH_2-$	59 (25 mm)	59 (25 mm)	67	[3]
III	$(CH_3)_2CHCH_2CH_2-$	57-62 (8 mm)	—	69	—
IV	$n\text{-}C_8H_{17}-$	125-126 (12 mm)	125-126 (12 mm)	72	[5]
V		105 (20 mm)	115-117 (30 mm)	74	[7]
VI	$CH_2{=}CH-CH_2-$	48-50 (12 mm)	—	75	—
VII		225-226	225-226	78	[9]
VIII	Cl 	135-136 (15 mm)	142 (17 mm)	93	[10]
IX	Br 	154 (12 mm)	—	85	—
X	CH_3O 	159-160 (20 mm)	—	86	—
XI	 OCH_3	151 (20 mm)	—	80	—
XII	 CH_2-	105-107 (5 mm)	81 (0.2 mm)	51	[13]

In connection with the interference encountered in nitration of 2-alkoxymethylbenzthiazoles with branched carbon chains, the author synthesized the corresponding 2-alkoxymethyl-, as well as the 2-aryloxymethyl-6-nitrobenzthiazoles, according to scheme II, by condensing 5-nitro-2-aminophenylmercaptan with alkoxy and aryloxyacetic acid chloroanhydrides.

A large number of alkoxy- and aryloxyacetic acid chloroanhydrides are described in the literature, the remaining being synthesized by the author, for the first time; they were not analyzed, but were identified in the form of condensation products with 5-nitro-2-aminophenylmercaptan. The boiling points and yields of these chloroanhydrides are given in Table 3.

5-Nitro-2-aminophenylmercaptan has received but little study. It was obtained for the first time by Mylius by splitting 6-nitrobenzthiazole with alcoholic alkali [22], and then by Jacobson and Kwaysser by splitting 2-oxy-5-nitrobenzthiazole with aqueous ammonia in a sealed tube [23].

TABLE 4

2-Alkoxymethyl- and 2-Aryloxymethyl-6-nitrobenzthiazoles of the General Formula 

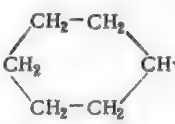
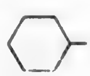
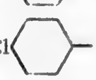
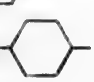
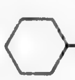
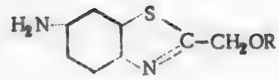
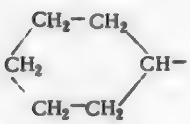
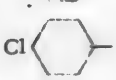
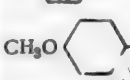
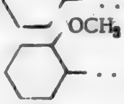
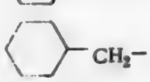
Preparation Number	R	Melting point	Yield (%)	Empirical formula	Analytical results: nitrogen (%) found	nitrogen (%) calc'd	sulfur (%) found	sulfur (%) calc'd
I	CH_3-	137-138°	64	$C_9H_8O_3N_2S$	12.45 12.44	12.50	14.38 14.39	14.28
II	CH_3CH_2-	111.5	70	$C_{10}H_{10}O_3N_2S$	11.48 11.56	11.76	12.96 12.87	13.44
III	$CH_3CH_2CH_2-$	72	35	$C_{11}H_{12}O_3N_2S$	11.22 11.30	11.11	12.74 12.67	12.69
IV	CH_3 $>CH-$ CH_3	101.4	25	$C_{11}H_{12}O_3N_2S$	10.90 10.98	11.11	12.66 12.60	12.69
V	$CH_3CH_2CH_2CH_2-$	83-84	66	$C_{12}H_{14}O_3N_2S$	10.67 10.75	10.52	12.19 12.38	12.02
VI	CH_3 $>CHCH_2-$ . . . . . CH_3	86	58	$C_{12}H_{14}O_3N_2S$	10.52 10.56	10.77	12.17 12.28	12.30
VII	CH_3 $>CHCH_2CH_2-$ . . . CH_3	63	25	$C_{13}H_{16}O_3N_2S$	10.08 9.89	10.00	11.52 11.51	11.42
VIII	n-$C_8H_{17}-$	69	45	$C_{16}H_{22}O_3N_2S$	8.65 8.78	8.69	10.05 10.03	9.93
IX		96-97	58	$C_{14}H_{16}O_3N_2S$	9.44 9.28	9.58	10.68 10.71	10.95
X	$CH_2=CH-CH_2-$	69	41	$C_{11}H_{10}O_3N_2S$	11.17 11.10	11.20	12.66 12.70	12.80
XI		161-162	84	$C_{14}H_{10}O_3N_2S$	9.60 9.50	9.79	10.86 10.96	11.18
XII	Cl 	153-154	80	$C_{14}H_9O_3N_2SCl$	8.62	8.73	–	–
XIII	Br 	167-168	86	$C_{14}H_9O_3N_2SBr$	7.69 7.71	7.67	8.97	8.76
XIV	CH_3O- 	144-145	82	$C_{15}H_{12}O_4N_2S$	8.88 8.72	8.86	10.02 10.09	10.12
XV	 OCH_3	120-121	51	$C_{15}H_{12}O_4N_2S$	8.90 8.72	8.86	10.24 10.11	10.12
XVI	 CH_2-	75-76	70	$C_{15}H_{12}O_3N_2S$	9.13 9.09	9.33	10.78 10.55	10.66

TABLE 5

2-Alkoxymethyl- and 2-Aryloxymethyl-6-aminobenzthiazoles of the General Formula 

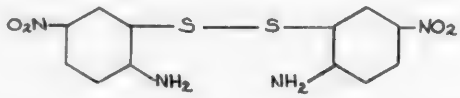
Preparation Number	R	Base				
		Melting point	Yield (%)	Empirical formula	Analytical: nitrogen (%) found	Analytical: nitrogen (%) calculated
I	CH_3-	–	–	–	–	–
II	CH_3CH_2-	–	–	–	–	–
III	$CH_3CH_2CH_2-$	–	–	–	–	–
IV	$CH_3CH_2CH_2CH_2-$	–	–	–	–	–
V	$\genfrac{}{}{0pt}{}{CH_3}{CH_3}\!>CHCH_2-$	–	–	–	–	–
VI	$\genfrac{}{}{0pt}{}{CH_3}{CH_3}\!>CHCH_2CH_2-$	–	–	–	–	–
VII	$n-C_8H_{17}-$	–	–	–	–	–
VIII		108°	68	$C_{14}H_{18}ON_2S$	10.47 10.49	10.67
IX		147-148	50	$C_{14}H_{12}ON_2S$	11.02 11.10	10.94
X		173	75	$C_{14}H_{11}ON_2SCl$	9.47 9.56	9.62
XI		181-182.5	83	$C_{14}H_{11}ON_2SBr$	8.50 8.53	8.36
XII		148	88	$C_{15}H_{14}O_2N_2S$	9.77 9.79	9.79
XIII		157.5	72	$C_{15}H_{14}O_2N_2S$	9.86 9.85	9.79
XIV	 . . .	–	–	–	–	–

Base		Hydrochloride					
results		Melting point	Empirical formula	Analytical results			
sulfur (%)				nitrogen (%)		chlorine (%)	
found	calculated			found	calculated	found	calculated
–	–	247° (decomp)	$C_9H_{11}ON_2SCl$	12.33 12.23	12.14	15.44 15.49	15.40
–	–	215 (decomp)	$C_{10}H_{13}ON_2SCl$	11.48 11.32	11.45	14.55	14.53
–	–	208-210 (decomp)	$C_{11}H_{15}ON_2SCl$	10.90 10.79	10.83	13.56 13.59	13.73
–	–	204 (decomp)	$C_{12}H_{17}ON_2SCl$	10.23 10.40	10.27	Sulfur 11.89	11.74
–	–	206-207 (decomp)	$C_{12}H_{17}ON_2SCl$	10.69 10.56	10.27	–	–
–	–	208-209 (decomp)	$C_{13}H_{19}ON_2SCl$	9.36 9.58	9.77	–	–
–	–	187 (decomp)	$C_{16}H_{25}ON_2SCl$	8.60 8.49	8.52	10.76 10.90	10.80
11.93 11.97	12.21	–	–	–	–	–	–
12.37 12.28	12.50	211-212	$C_{14}H_{13}ON_2SCl$	9.63 9.66	9.57	12.04 12.06	12.13
	–	231-232	$C_{14}H_{12}ON_2SCl_2$	8.78 8.67	8.56	21.46	21.71
Bromine 23.83 24.01	23.88	238-238.5	$C_{14}H_{12}ON_2SClBr$	7.36 7.48	7.53	–	–
11.08 11.19	11.19	217 (decomp)	$C_{15}H_{14}ON_2SCl$	8.96	8.68	10.69 10.65	11.00
11.00 11.05	11.19	189	$C_{15}H_{14}O_2N_2SCl$	8.07	8.68	–	–
–	–	207-208 (decomp)	$C_{15}H_{15}ON_2SCl$	9.17 9.30	9.13	11.65 11.72	11.61

The author obtained 5-nitro-2-aminophenylmercaptan in 83% yield by heating 2-oxy-6-nitrobenzthiazole with aqueous ammonia in an autoclave. The m.p. was 89-90° (Jacobson and Kwaysser indicated a yield of about 60%. m.p. 83-84°).

To identify the 5-nitro-2-aminophenylmercaptan obtained by the author, it was condensed with formic acid. The product with m.p. 176-177° was isolated in quantitative yield, which did not produce depression in a mixed sample with 6-nitrobenzthiazole obtained by nitration of benzthiazole. A product with m.p. 164° was isolated by condensation with acetyl chloride, and gave no depression in a mixed sample with 2-methyl-6-nitrobenzthiazole, obtained by nitration of 2-methylbenzthiazole.

Attempts to carry out condensation of 5-nitro-2-aminophenylmercaptan with alkoxy- and aryloxy-acetic acids by heating the components in benzene or toluene did not lead to positive results. Each time a disulfide separated with a m.p. of 237-238°:



synthesized for the first time by Jacobson and Kwaysser by oxidation of 5-nitro-2-aminophenylmercaptan. Its formation as a result of heating with alkoxy and aryloxyacetic acids is an indication of its tendency to auto-oxidation.

It was found that 2-alkoxymethyl-6-nitrobenzthiazoles are formed very readily at room temperature, by interacting 5-nitro-2-aminophenylmercaptan with chloranhydrides of alkoxyacetic acids. In these reactions, disulfide is found to be only a side product.

Upon interacting 5-nitro-2-aminophenylmercaptan with the chloroanhydride of aryloxyacetic acids in pyridine, or without solvent, products are formed, whose analysis corresponds to the diacyl derivatives of 5-nitro-2-aminophenylmercaptan.

After arranging condensation experiments in the presence of anhydrous zinc chloride, reaction went in the desired direction and a series of 2-aryloxy-6-nitrobenzthiazoles was obtained.

New bases, resulting from condensation of 5-nitro-2-aminophenylmercaptans with alkoxy- and aryloxyacetic acid chloroanhydrides, are given in Table 4. Preparations I, II, III, and IV were obtained by nitration of the corresponding 2-alkoxymethylbenzthiazoles. 2-Alkoxymethyl- and 2-aryloxymethyl-6-nitrobenzthiazoles, were in the form of light yellow crystals, soluble in organic solvents, wherein the 2-aryloxy derivatives are much less soluble than the 2-alkoxymethyl-6-nitrobenzthiazoles.

Reduction of these nitro derivatives was carried out with iron shavings in a water-alcohol medium, in the presence of a small amount of acetic acid.

2-Alkoxymethyl-6-aminobenzthiazoles are liquids. They were identified as their hydrochlorides. Acetyl derivatives were obtained for some of them. The 2-aryloxymethyl-6-aminobenzthiazoles are well-crystallizing compounds, with boiling points above 100°. Yields, melting points, and analyses for the isolated amines are given in Table 5.

The amines were converted into the corresponding hydrochlorides and acetal derivatives. Analyses and melting points of the 2-alkoxymethyl- and 2-aryloxymethyl-6-aminobenzthiazole hydrochlorides are given in Table 5. The salts are in the form of colorless crystals. The 2-alkoxymethyl-6-aminobenzthiazole hydrochlorides are readily soluble in water, alcohol and acetone; the aryloxymethyl-5-aminobenzthiazole hydrochlorides are very poorly soluble in water, and in alcohol, they dissolve with greater difficulty than with the alkoxy salt derivative.

2-Alkoxymethyl-6-aminobenzthiazole hydrochlorides, in contrast to the 2-alkoxy-6-aminobenzthiazole hydrochlorides [2], are found to be stable compounds. The author did not observe noticeable desalkylation when synthesizing them.

The acetyl derivatives of 2-alkoxymethyl- and 2-aryloxymethyl-6-aminobenzthiazoles are given in Table 6. They are in the form of colorless crystals. 2-Alkoxymethyl-6-aminobenzthiazoles, when treated with acetic anhydride, give liquid products which are evidently mixtures, and therefore in only two cases was it possible to isolate pure crystalline acetyl derivatives. 2-Aryloxymethyl-6-aminobenzthiazoles form readily crystallizing substances, and were recrystallized from benzene.

EXPERIMENTAL

o-Aminophenylmercaptan. Obtained from Captax, according to the method developed by Kiprianov and Ushenko [24].

Alkoxyacetic Acids. (See Table 1). Prepared by boiling solutions of the alcoholates in the corresponding alcohols, with a small excess of chloroacetic acid.

Aryloxyacetic Acids. (See Table 1). Prepared by boiling the corresponding phenols with chloroacetic acid in the calculated amount of 10% sodium hydroxide solution.

Alkoxy- and Aryloxyacetic Acid Chloroanhydrides (See Table 3). Obtained by heating the acids with 15% excess of thionyl chloride on a water bath at 60° for 2 hours. After distilling off the thionyl chloride excess, the chloroanhydrides were distilled in vacuo.

Jacobson and Kwaysser obtained 5-nitro-2-aminophenylmercaptan, starting from phenyl mustard oil, which was converted via the urethane into 2-oxybenzthiazole.

The author obtained 2-oxybenzthiazole from Captax in very good yield according to the method proposed by Efros and Davidenkov [25].

2-Oxy-6-nitrobenzthiazole was prepared as follows: 45 ml of nitric acid (d 1.38) in 45 ml of concentrated sulfuric acid mixture was introduced dropwise, and with mechanical stirring at 5 - 10°, was slowly added to a solution of 60.4 g (0.4 mole) of 2-oxybenzthiazole in 100 ml of concentrated sulfuric acid. The nitrating mixture was added over a period of 45 minutes, and after completion of addition of the mixture, the reaction mass was stirred for 30 minutes at room temperature, and then poured onto chipped ice. The resulting precipitate was filtered off, washed several times with water, dried, and recrystallized from glacial acetic acid. The m.p. was 248°, yield of recrystallized product being 42 g (54%).

A suspension of 59 g of 2-oxy-6-nitrobenzthiazole in 750 ml of ammonia (d 0.950) was heated in an autoclave with a stirrer at 150° for 4 hours. After cooling, the resulting dark-red, ammoniacal solution was filtered, the filtrate neutralized with dilute hydrochloric acid, with external cooling. The resulting light-yellow precipitate was filtered off, washed with water, thoroughly pressed out, and dried in a vacuum desiccator over sulfuric acid. The m.p. was 84 - 85°, yield 42.3 g (83%). After recrystallization from aqueous alcohol, the melting point of 5-nitro-2-aminophenylmercaptan was 89 - 90°.

2-Alkoxymethylbenzthiazoles. (Table 2).

A mixture of 10 g (0.08 mole) of o-aminophenylmercaptan and 0.1 mole of the corresponding alkoxyacetic acid was heated on an oil bath at 135 - 140° for 3 - 4 hours. After cooling, 5 ml of 10% sodium hydroxide was added and the oil which separated was extracted with ether. The ether solution was dried over anhydrous potash, and after distilling off the ether, it was distilled in vacuo.

Nitration of 2-Alkoxymethylbenzthiazoles.

5 ml of nitric acid (d 1.38) was added dropwise at 5 - 10°, with mechanical stirring, for a period of 30 minutes, to a solution of 5.7 g of 2-methoxymethylbenzthiazole in 25 ml of concentrated sulfuric acid. After stirring for 1 hour at room temperature, the reaction mass was poured into ice water. The resulting precipitate was filtered, washed with water, dried, and recrystallized from alcohol. Preparations II, III and V (Table 4) were similarly prepared.

Determination of the Nitro Group Position in Nitration Products of 2-Alkoxymethylbenzthiazoles. 1) 5% potassium permanganate (30 ml) and 5 ml of 5% sodium hydroxide were added to 0.5 g of 2-alkoxymethylbenzthiazole nitroderivative, and the mixture boiled for 1 hour. After filtration of the reaction mixture, the filtrate was decolorized with a small amount of perhydrol, again filtered, and neutralized with dilute hydrochloric acid. A precipitate with m.p. 174° separated from the solution, and did not give depression when mixed with a sample of 6-nitrobenzthiazole, obtained by nitration of benzthiazole.

2) Upon nitrating 2-isopropoxymethyl-, 2-isobutoxymethyl-, 2-isoamyloxymethyl- and 2-allyloxymethylbenzthiazoles under the same conditions, as were used for nitration of 2-alkoxymethylbenzthiazoles with a normal chain of carbon atoms, the precipitate which resulted in all cases possessed one and the same m.p. of 167-168°. Analysis of this product for nitrogen indicated that it corresponded to 2-oxymethylnitrobenzthiazole.

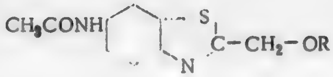
Found %: N 13.18, 13.01. $C_8H_6O_3N_2S$. Calculated %: N 13.33.

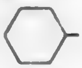
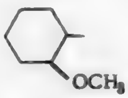
Determination of the melting point on a mixed sample with 2-oxymethyl-6-nitrobenzthiazole, obtained according to Zubarovsky by nitration of 2-oxymethylbenzthiazole, did not produce depression.

3) 2.35 g of isoamyloxybenzthiazole in 8 ml of acetic anhydride was added with stirring, at room temperature, to a solution of 1 ml of nitric acid (d 1.5) in 15 ml of glacial acetic acid. Having completed addition of

TABLE 6

Acetyl Derivatives of 2-Alkoxymethyl- and 2-Aryloxymethyl-6-aminobenzthiazole of the General Forumla:



Preparation No.	R	Melting point	Empirical formula	Analytical results: Nitrogen (%) Found	Nitrogen (%) Calc'd	Sulfur (%) Found	Sulfur (%) Calc'd
I	CH_3CH_2-	108 - 109°	$C_{12}H_{14}O_2N_2S$	11.10 11.02	11.20	12.68 12.74	12.80
II	$CH_3CH_2CH_2CH_2-$	92 - 93	$C_{14}H_{18}O_2N_2S$	10.06 10.26	10.07	11.47 11.56	11.51
III		160	$C_{16}H_{14}O_2N_2S$	9.25 9.16	9.39	10.63 10.56	10.73
						Chlorine	
IV	Cl 	200	$C_{16}H_{13}O_2N_2SCl$	8.49 8.42	8.42	10.66 10.74	10.68
V	Br 	199	$C_{16}H_{13}O_2N_2SBr$	7.53 7.36	7.45	–	–
VI	CH_3O 	166	$C_{17}H_{16}O_3N_2S$	8.28 8.35	8.53	–	–
VII		145	$C_{17}H_{16}O_3N_2S$	8.44 8.49	8.53	–	–

thiazole, the reaction mixture was heated for 15 minutes at 50° and was left for 1 hour at room temperature. Upon pouring into ice water, a yellow oil precipitated, which was extracted with ether. The ether solution was dried with sodium sulfate, and after distilling off the ether, the residue was distilled in vacuo at 6 mm and 100 - 135°. The major portion of distillate solidified and was recrystallized from petroleum ether. M.p. 74°. Analysis for nitrogen and sulfur corresponded to benzthiazolylaldehyde, and not to the expected 2-isoamyloxymethyl-6-nitrobenzthiazole.

Found %: N 8.62, 8.46; S 19.77, 19.72. C_8H_5ONS. Calculated %: N 8.58; S 19.73.

Determination of the melting point of a sample mixed with 2-benzthiazolylaldehyde* did not give depression.

Nitrationof 2-isopropoxymethyl-, 2-isobutoxymethyl-, and 2-isoallyloxymethylbenzthiazoles led to the same results under conditions indicated above, i.e.,with formation of 2-benzthiazolylaldehyde in 30 - 35% yield.

Condensation of 5-Nitro-2-aminophenylmercaptan with Alkoxyacetic Acid Chloroanhydrides.

3.4 g (0.02 mole) of 5-nitro-2-aminophenylmercaptan was ground throughly with 0.021 mole (slight excess) of alkoxyacetic acid chloroanhydride. Spontaneous evolution of heat was observed, and the yellow color of 5-nitro-2-aminophenylmercaptan changed to orange. The mixture was left standing for 10 minutes, and was then suspended in 20 ml of 5% sodium hydroxide solution. The precipitate was filtered off, washed with water, and after drying in air, was recrystallized from dilute alcohol. Preparations IV, VI, VII, VIII and IX (Table 4) were obtained in similar fashion.

Formation of a substance, poorly soluble in alcohol, was observed as a side product of the reaction. After crystallization fom glacial acetic acid, the substance melted at 237 - 238°. This melting point corresponded to the melting point of the disulfide. Analysis for nitrogen confirmed this assumption.

Found %: N 16.40. $C_{12}H_{10}O_4N_4S_2$. Calculated %: N 16.57.

Condensation of 5-Nitro-2-aminophenylmercaptan with Aryloxyacetic Acid Chloroanhydrides.

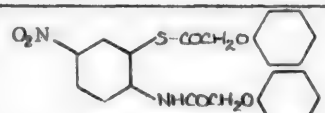
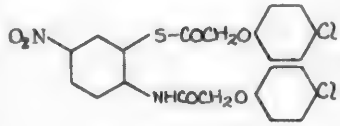
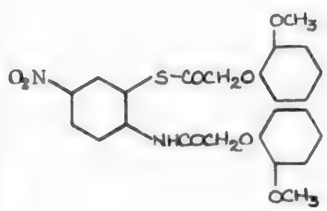
1) 1.7 g (0.01 mole) of 5-nitro-2-aminophenylmercaptan was ground thoroughly with the chloroanhydrides (0.012 mole) of phenoxyacetic, p-chlorophenoxyacetic and o-methoxyphenoxyacetic acids; spontaneous evolution

* 2-Benzthiazolylaldehyde was kindly furnished to us by V. M. Zubrovsky.

of heat was observed, evolution of hydrogen chloride, and a change in color of 5-nitro-2-aminophenylmercaptan. After standing for some time, the reaction mixture was suspended in 20 ml of 5% sodium hydroxide solution, the precipitate filtered off, washed with water, and after drying, was recrystallized from acetic acid, since the precipitate was insoluble in alcohol. Analyses of the synthesized preparations corresponded to the acylation products, whose assumed structure is given in Table 7.

2) 3.4 g (0.02 mole) of 5-nitro-2-aminophenylmercaptan was suspended in dry ether, and 0.022 mole of aryloxyacetic acid chloroanhydride solution in ether and 3 g of anhydrous zinc chloride, added to the suspension; boiling up of the reaction mixture and conversion to a red color was observed. The reaction mixture was then boiled gently on a water bath for 30 minutes, the ether distilled off, the residue suspended in water, filtered, washed with 5% sodium hydroxide solution, and then water. After drying, the precipitate of 2-aryloxymethyl-6-

TABLE 7

Prep. No.	Structure	Melting point	Empirical formula	Nitrogen (in %) Found	Nitrogen (in %) Calc'd	Sulfur (in %) Found	Sulfur (in %) Calc'd
I		173-174°	$C_{22}H_{18}O_6N_2S$	6.35 6.60	6.39 –	7.21 7.25	7.30 –
						Chlorine	
II		204	$C_{22}H_{16}O_6N_2SCl_2$	5.38 5.34	5.52 –	13.85 13.97	14.00 –
III		149-150	$C_{24}H_{22}O_8N_2S$	5.96 6.06	5.62 –	–	–

nitrobenzthiazole was recrystallized from glacial acetic acid. The preparations obtained in this manner are given in Table 4 (XI-XVI).

<u>2-Alkoxymethyl- and 2-Aryloxymethyl-6-aminobenzthiazoles (Table 5).</u>

15 g of iron shavings and 10 ml of 20% acetic acid were added to a boiling solution of 0.015 mole of 2-alkoxymethyl- or 2-aryloxymethyl-6-nitrobenzthiazole in 50 ml of alcohol (in the case of poorly-soluble nitrocompounds, a suspension was used). The mixture was boiled on a water bath for 1 hour stirring, and 20 ml of water added in portions, over this period of time. Boiling on a water bath was continued for another hour, and the reaction mixture was then filtered. The filtrate was diluted with water. In those cases where an oily product separated upon dilution with water, the product was extracted with ether, dried with anhydrous sodium sulfate, and after distilling off the ether, the remaining amine identified in the form of its hydrochloride and acetyl derivatives. In those cases where the amine precipitated in the form of a crystalline precipitate, it was filtered and recrystallized from dilute alcohol. The amines were converted into the hydrochlorides when their alcoholic solutions were combined with the ether solution of hydrogen chloride. Recrystallized from alcohol by addition of a small amount of ether.

The acetyl derivatives were obtained by short boiling of the amine with acetic anhydride (Table 6).

SUMMARY

1. A number of 2-alkoxymethylbenzthiazoles have been obtained.

2. 2-Alkoxymethyl-6-nitrobenzthiazoles are formed upon nitrating 2-alkoxymethylbenzthiazoles containing an alkyl group with the normal chain of carbon atoms.

3. Upon nitrating 2-alkoxymethylbenzthiazoles containing an alkyl with branched chain carbon atoms, or a short chain, with a mixture of nitric and sulfuric acids, simultaneous desalkylation occurs along with the nitration process. 2-Oxy-6-nitrobenzthiazole is formed.

4. Upon nitrating the same alkoxymethylbenzthiazoles in acetic anhydride medium, the alkoxymethyl group oxidizes to an aldehyde group, and 2-benzthiazolylaldehyde is formed.

5. Diacyl derivatives are formed upon interaction of 5-nitro-2-aminophenylmercaptans with the chloroanhydrides of aryloxyacetic acids in the absence of zinc chloride.

6. A number of 2-alkoxymethyl- and 2-aryloxymethyl-6-nitrobenzthiazoles have been prepared by condensing 5-nitro-2-aminophenylmercaptan with alkoxy- and aryloxyacetic acid chloroanhydrides, in the presence of anhydrous zinc chloride.

7. Upon reducing 2-alkoxymethyl- and 2-aryloxymethyl-6-nitrobenzthiazoles, the corresponding amines have been prepared, which have been converted into the hydrochloride and acetyl derivatives.

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DIRECT IODINATION OF BENZENE, TOLUENE, CHLOROBENZENE, IODOBENZENE AND p-NITROTOLUENE

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Upon halogenating benzene with elementary iodine in the presence of nitric acid (d 1.5) [1], nitro compounds result in addition to the main reaction product of iodobenzene. The recommended method for purifying by reduction does not give satisfactory results. The iodobenzene which results in practice contains traces of nitrobenzene. Duration of the process, and the use of nitric acid of specific gravity 1.5 can also be included among shortcomings of this process.

Directions are also found in the literature for the use of other relatively ineffective oxidants in the iodination of benzene [2]. Recently, a synthetic method for producing iodobenzene from benzene and iodine in the presence of relatively costly materials such as the silver salts of perchloric acid [3], of sulfuric acid [4] and of trifluoroacetic acid [5] have been described in the literature. Despite this fact, iodobenzene is synthesized chiefly from aniline and not by direct iodination of benzene.

Tronov and Novikov [6] synthesized m-iodobenzoic acid and m-iodobenzaldehyde by direct iodination of benzoic acid and benzaldehyde in the presence of a standard nitrating mixture.

It was of considerable interest to test a sulfuric-nitric mixture upon iodination reactions of benzene and other aromatic compounds.

As a result of arranging experiments, iodobenzene, a mixture of o- and p-iodotoluenes, p-diiodobenzene, p-iodochlorobenzene and 2-iodo-4-nitrotoluene were prepared free from nitro compound impurities.

EXPERIMENTAL*

Iodination of Benzene. A pre-cooled mixture, preared in advance, composed of glacial acetic acid (20 ml) and sulfuric acid (5.5 ml) was placed in a three-necked round-bottomed flask containing iodine (6.35 g) and benzene (7 ml). 1.6 ml of nitric acid (d 1.4) was gradually added, with vigorous mechanical stirring, to the reaction vessel, 46°, over a period of 45 minutes, from a buret. Heating was continued for another 15 minutes. The color of the reaction mixture was dark-brown.

The mixture was diluted with water, the resulting heavy oily liquid separated from the aqueous acid layer, washed free of acids, treated with sodium sulfite and water. The oil was fractionated after being dried over calcium chloride. Benzene in unchanged form distilled off first, and then at 186 - 187.5°, iodobenzene distilled off. A small residue crystallized out in the distilling flask upon cooling (apparently diiodobenzene). The yield of iodobenzene was 80% (8.0 g) on the basis of iodine taken for reaction.

Found (according to Stepanov) %: I 63.0. C_6H_5I. Calculated %: I 62.3.

Test for nitrogen after decomposition with sodium was negative. Treatment with stannous chloride and hydrochloric acid, with subsequent addition of sodium nitrite and β-naphthol did not produce a colored solution, indicating absence of the nitro group.

An increase in the amount of nitric acid, a decrease in the amount of glacial acetic acid, and an increase in the reaction temperature, promote formation of nitrobenzene. Slow stirring, or the absence of sulfuric acid, lower considerably the yield of product. Addition of a small amount of urea (0.3 - 0.5g) made it possible to carry out the reaction without withdrawal or trapping of nitrogen oxides.

Iodination of Toluene. A mixture of 8.5 ml of toluene, 6.35 g of iodine, 5.5 ml of sulfuric acid, and 20 ml of glacial acetic acid was heated at 45°. 1.3 ml of nitric acid was introduced into the flask with vigorous stirring, over a period of 35 minutes. Reaction time was 4 minutes. The oily reaction product, after drying, was distilled under standard conditions. At 207-212° 9.4 g (95 %) of o- and p-iodotoluene mixture was collected. A

* V.A. Sensky, P. F. Koronin, B. F. Lagerev, A. N. Polyakova, and K. S. Savelyeva participated in the experimental portion of this work.

second distillationgave two fractions: 1st fraction – b.p. 205-209°, 1.5 g; 2nd fraction – b.p. 209-210°, 7.8 g (70 %). Upon oxidizing the 2nd fraction with dilute nitric acid at 135°, p-iodobenzoic acid resulted with m.p. 269°. Qualitative test for nitrogen was negative.

Found (according to Stepanov) %: I 58.4. C_7H_7I. Calculated %: I 58.2.

Iodination of Benzene. Nitric acid (2.7 ml0 was added with mechanical stirring over a period of 25 minutes to a mixture of 5.6 ml of iodobenzene, 6.35 g of iodine, 5.6 ml of sulfuric acid, 30 ml of glacial acetic acid and 4 ml of carbon tetrachloride at 115°. Reaction lasted for 35 minutes. The reaction mixture was diluted with water, and solid diiodobenzene separated, was washed with water and alcohol (5 ml). The yield was 8.9 g (55%). M.p. was 130-131° (from ethanol). 4 g of oil (20%) remained in the residue. This was apparently o-diiodobenzene.

Found (according to Stepanov) %: I 76.4. $C_6H_4I_2$. Calculated %: I 76.9.

Iodination of Chlorobenzene. Carried out under the same conditions as for iodobenzene. p-Chloroiodobenzene resulted in 40 % yield. M.p. was 55-56°. The o-isomer was detected in the form of an oil.

Iodination of p-Nitrotoluene. 6.85 g of nitrotoluene, 6.35 g of iodine, 11.2 ml of sulfuric acid, 3.4 ml of nitric acid, 6 ml of carbon tetrachloride and 15 ml of glacial acetic acid. Temperature of the reaction was 100°, time 3 hours. The nitric acid was added uniformly over a period of 35 minutes. After reaction the mixture was distilled with steam, and the unreacted iodine and p-nitrotoluene removed. The yield of iodonitrotoluene was 70 %, m.p. 58° (from methanol).

Found (according to Stepanov) %: I 47.1. $C_7H_6NO_2I$. Calculated %: I 48.2.

SUMMARY

1. Sulfuric-nitric acid mixture can be used successfully for the iodination reaction of many aromatic compounds.

2. By carrying out a direct iodination under strictly specified conditions, and without excess of nitric acid, iodo derivatives without contaminating nitro compounds can be prepared.

3. There have been prepared by direct iodination reaction in the presence of nitrating mixture: iodobenzene, p-diiodobenzene, a mixture of o- and p-iodotoluenes, p-chloroiodobenzene and 2-iodo-4-nitrotoluene.

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CATALYTIC CONVERSION OF HALOGEN DERIVATIVES IN THE AROMATIC SERIES

I. ISOMERISM OF THE MONOCHLORONAPHTHALENES

N. N. Vorozhtsov, Jr., and A. M. Beskin*

The isomerization reaction for halogen compounds of the aliphatic series was described back in 1875 by Eltekov [1], and later by Favorsky [2], who studied it with considerable thoroughness.

Possibility of isomerization was also demonstrated for some halogen derivatives of the aromatic series; however, no one has, as yet, succeeded in obtaining satisfactory yields of isomerization products, in particular as regards the most interesting halogen derivatives.

Thus, Roux [3], for the first time succeeded in isomerizing 1-bromo- and 1-chloronaphthalenes by reacting these substances with aluminum chloride in carbon disulfide. 2-Bromo- and 2-chloro-naphthalenes, respectively, were isolated in small amounts from the reaction mass, as well as naphthalene and dihalogen derivatives, in addition to the initial monohalogen compound of naphthalene.

Fischer and Clark [4] demonstrated later that when certain metals (Sb, Mo, Ni, W, Cr) are added to aluminum chloride, the yield of 2-bromonaphthalene can be increased to 25% (yield being 9.1% without these additives).

Meyer and Schiffner [5] isolated about 1% of not very pure 2-bromonaphthalene by passing vapors of 1-bromonaphthalene over silica gel.

Wibaut and coworkers [6] established that isomerization of 1-bromonaphthalene occurs upon heating it with ferric chloride in a stream of hydrogen bromide at 150°. The resulting mixture contained 60% 2-bromonaphthalene and 40% 1-bromonaphthalene. Noticeable quantitites of naphthalene and dibromonaphthalene were formed simultaneously. It was established that the isomerization reaction is reversible; a mixture of the same composition was obtained from 2-bromonaphthalene. Similar results were obtained by passing vapors of bromonaphthalene and hydrogen bromide over ferric chloride placed in pumice. In the opinion of the Dutch investigators, isomerization is effected by reversibility of the bromination process.

As is known, 1-chloronaphthalene is predominantly formed upon chlorination of naphthalene in the liquid phase, and about 10% 2-chloronaphthalene [7] is also present. Wibaut and Bloem [8] have recently demonstrated that when chlorination of naphthalene is carried out at a temperature above 350°, there is formed a mixture of monochloronaphthalenes, containing almost 50% of 2-chloronaphthalene. The yield of chloronaphthalenes mixture in this case is not very high (less than 50% of the naphthalene entering into reaction).

The authors have investigated the synthesis of 2-chloronaphthalene by the method of catalytic vapor phase isomerization of 1-chloronaphthalene.

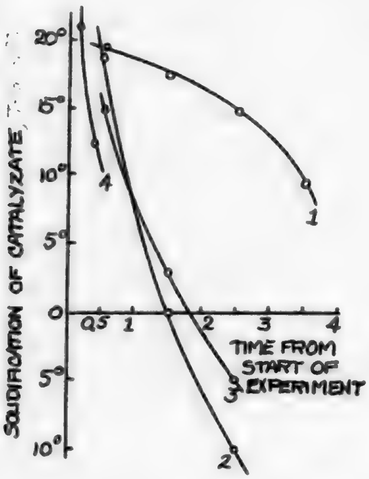
Testing of various catalysts has indicated that at 400° chloronaphthalene does not change noticeably when passed with a stream of hydrogen chloride over silica gel and phosphoric acid on kieselguhr. At the same time, use of synthetic aluminosilicate catalyst and aluminum oxide under the same conditions leads to considerable isomerization of 1-chloronaphthalene. The catalyzate which resulted consisted of a mixture of 1- and 2-chloronaphthalenes, containing about 50% of 2-chloronaphthalene. It was established that the presence of hydrogen chloride has a pronounced influence upon the isomerization process. Thus, on aluminum oxide, in a stream of carbon dioxide, isomerization does not occur at all.

Upon passing chloronaphthalene over aluminosilicate catalyst, isomerization proceeds in a stream of carbon dioxide, and without any gas at all. However, with hydrogen chloride, the catalyst rapidly (after 15-30 minutes) decreases in activity. In the presence of hydrogen chloride, however, isomerization can be carried on for 2-3 hours (see Figure).

Decrease in catalyst activity is related to the accumulation of high-molecular-weight chloronaphthalene decomposition products, formed as by-products, upon the catalyst. After 15 minutes of work, the catalyst contains

* Deceased.

about 2 - 2.5% carbon. The process of formation of these by-products apparently occurs with splitting off of hydrogen chloride, since the catalyzate possessed some (up to 0.04 - 0.08%) HCl, and the C:Cl ratio accumulating on the catalyst is higher than in the initial chloronaphthalene.



Modification of the Extent of Isomerization with Respect to Duration of Catalyst Activity.

1) In a stream of HCl; 2) in a stream of CO_2; 3) and 4) without gas: a) solidification temperature of catalyzate; b) time from start of experiment.

The favorable effect of hydrogen chloride upon the stability of the catalyst is apparently explainable by the fact that a high concentration of hydrogen chloride inhibits the pyrolysis process because of the fact that one stage of the process occurring with rupture of hydrogen chloride is reversible. The effect of hydrogen chloride on the catalyst for the given case is apparently identical with the effect of hydrogen, which ensures stability of catalyst in the aromatizing process; in this case the pyrolysis process occurs with cleavage of hydrogen [9].

Pyrolysis in the isomerization process for chloronaphthalene proceeds on a relatively small scale. The yield of catalyzate constitutes not less than 95% of the chloronaphthalene passed through. Activity of the catalyst can be completely regenerated by heating it in a stream of air.

Isomerization of 1-chloronaphthalene is a reversible process. This situation indicates first of all that repeated passage of catalyzate over catalyst does not lead to an increased yield of 2-chloronaphthalene. Reversibility was also proved by direct experiment: passage of 2-chloronaphthalene over aluminosilicate in a stream of hydrogen chloride at 350-400° gave a mixture of the 1- and 2-chloronaphthalenes, almost identical in composition to the one resulting from isomerization of 1-chloronaphthalene.

Investigation of 1-chloronaphthalene isomerization on aluminum oxide in a stream of hydrogen chloride indicated that hydrogen chloride reacts to a certain degree with the catalyst, gradually increasing its activity. Best results are obtained by preliminary treatment of Al_2O_3 at 350° with hydrogen chloride for 1.5 hours. The catalyst treated in such manner retains its activity (when working with a stream of hydrogen chloride) for 7 hours; in this case about 5% carbon accumulates on it. Catalyst activity can be regenerated by treating it with air and hydrogen chloride.

The optimal reaction temperature was found to be 350°, and the optimal mole ratio of HCl to $C_{10}H_7Cl$ equal to 3:1. In this case the solidification temperature for catalyzate was 23.8° (corresponding to a content of about 55% of the 2-isomer). Per liter of catalyst, 300-350 g. of 1-chloronaphthalene can be passed through in 1 hour.

The mother liquor, after separation of 2-chloronaphthalene, can be repeatedly returned in the process, without lowering the yield of catalyzate or changing its composition. Thus, it is possible to convert almost completely the 1-chloronaphthalene into 2-chloronaphthalene. Catalytic isomerization of 1-chloronaphthalene has been found a convenient method for preparing what up to the present time has been an almost inaccessible 2-chloronaphthalene.

EXPERIMENTAL

1-Chloronaphthalene was prepared by chlorination of naphthalene in benzene with subsequent distillation or fractionation on a dephlegmator of technical chloronaphthalene (GOST 2660-44).* The fraction with b.p. 252-258° and d_4^{15} 1.1954 - 1.2001 was used for the investigation. By analysis according to the concentration method [7], it was determined that the product contained little naphthalene (up to 1%) and dichloronaphthalene (up to 2%). The content of 2-chloronaphthalene as determined by solidification temperature of the product with pure 2-chloronaphthalene, was equal (in accordance with the literature data [7]) to 10.5%.

The catalyst was placed in a vertical, fire-resistant glass tube (24 mm in diameter), heated by an electric oven. The layer of catalyst (height 12-24 cm, volume 40-80 ml), was between two layers of glass, the upper of which (18 cm length) served for evaporation of the chloronaphthalene which was fed from a buret. The side outlet of the T-tube which connected the buret with the tube, served to feed in the gas. The lower end of the catalyst tube was joined to the receiver for liquid reaction products.

* All-Union State Standard.

As catalysts for the isomerization, silica gel, phosphoric acid on kieselguhr, aluminum oxide and synthetic aluminosilicate were tested.

Experiments were carried out at 400°, and with a supply of 3.8 - 3.9 g of chloronaphthalene and 120 ml of hydrogen chloride per hour per 80 ml of catalyst. Course of the conversion was followed by the change in solidification temperature of catalyzate (the initial chloronaphthalene did not freeze at −15°). Experimental results are given in Table 1.

TABLE 1

Experiment No.	Catalyst	1-Chloronaphthalene passed through (in g)	Wt. of catalyzate (in g)	Solidification temp. of cat.	Precipitate isolated upon cooling to −5°		Solidification temp. of mother liquor	2-Chloronaphthalene content in catalyzate (in %)
					Wt. (in g)	Melting point		
1	Aluminosilicate	20.5	16.40	+20°	3.9	46-47°	+9°	51.0
2	Aluminum oxide	20.0	16.80	+17	4.7	46-47	+5	48.5
3	Phosphoric acid on kieselguhr.	19.3	17.35	Does not freeze at −15°	0	—	—	—
4	Silica gel	20.0	18.30		0	—	—	—

After one recrystallization from alcohol of the precipitates isolated in Experiments 1 and 2, colorless, lustrous scales resulted, with m.p. 56-57°. M.p.'s of 56, 58, 60 and 61° [11] are indicated in the literature for 2-chloronaphthalene. A sample mixed with 2-chloronaphthalene prepared from 2-naphthylamine (m.p. 56-57°) melted at 56-57°.

Found %: C 73.74, 73.92; H 4.12, 4.12. $C_{10}H_7Cl$. Calculated %: C 73.86; H 4.34.

The boiling points of the mother liquors (245-260°) were close to the boiling point of original product, which indicated no noticeable disproportionation reactions. The mother liquors were apparently a mixture of 1- and 2-chloronaphthalenes and their composition can be determined by solidification curves for similar mixtures [7, 8].

Isomerization of 1-Chloronaphthalene in the Presence of Various Gases.

Comparative isomerization experiments on Al_2O_3 (80 ml) in the presence of hydrogen chloride and carbon dioxide at 350° were carried out. The rate of gas passage was 65 ml. per minute. The results are given in Table 2.

TABLE 2

Gas	Experiment time	Chloronaphthalene passed through (in g)	Solidification temperature of catalyzate	Content of 2-chloronaphthalene (in %)
Hydrogen chloride	5 hrs.	37.5	+ 21°	54
Carbon dioxide	4 hrs. 15 min.	15.1	Does not freeze at −15°	—

Hence, on aluminum oxide, the isomerization process for chloronaphthalene proceeds only in the presence of hydrogen chloride. In the presence of carbondioxide, despite a somewhat longer contact time, isomerization does not proceed.

The effects of various gases were studied in more detail when using the aluminosilicate catalyst. The nature of change in activity of the catalyst in the presence of various gases, and absence of gases, was determined by the change in solidification temperature of the catalyzate during the isomerization process. Experiments were carried out under the following conditions: temperature 400°; the volume of aluminosilicate catalyst was 40 ml, the feed of chloronaphthalene was 8 - 10 g per hour, HCl feed was 80 ml per minute, and the feed of carbon dioxide was 100 ml per minute. Experimental results are given in Table 3.

TABLE 3

Gas	Solidification temp. of the catalyzate, resulting within			
	1st hour	2nd hour	3rd hour	4th hour
Hydrogen chloride . . .	19.4°	17.8°	14.6°	9.2°
Carbon dioxide	18.5	0	− 10	
Without gas	14.6	3.2	− 5	

Table 3 indicates that the presence of hydrogen chloride is not required for isomerization of chloronaphthalene; it only slows down the deactivation process of the catalyst. Isomerization without gas (perhaps the most interesting one) can give good results with less work by the catalyst. Thus, at 400° and a feed rate of 21.6 g of chloronaphthalene per hour per 40 ml of catalyst for the first 15 minutes resulted in a solidification temperature up to +21°. Within the next 15 minutes, catalyzate solidification temperature of +15.6° resulted.

Catalyst which has lost its activity contains a considerable amount of chloronaphthalene decomposition products. For example, analysis of the catalyst which was worked for 15 minutes at 400° indicated a content of 2.07 % carbon and 0.32% chlorine (in another sample, 2.49% C and 0.59% Cl). It is of interest to note that the C:Cl ratio in the product accumulating on the catalyst is greater (4.5 - 6.5:1) than for chloronaphthalene (3.4:1). Consequently, decomposition of chloronaphthalene which occurs as a side reaction should proceed with cleavage of hydrogen chloride. Actually, the hydrogen chloride content of catalyzate amounted to 0.04 - 0.08% (determination carried out by titration with 0.1 N sodium hydroxide of catalyzate mixed with water). Decreasing the isomerization temperature to 350° gave a decreased hydrogen chloride content of 0.01 - 0.03% in the catalyzate. The yield of catalyzate fluctuated from 95.0 to 96.5% for the chloronaphthalene passed through (at 400°).

Activity of the aluminosilicate catalyst can be regenerated by standard procedure — passage of air through it. For the case given, it was necessary to pass air through for approximately 3 hours, at a rate of 0.2 - 0.5 liter per minute (for 40 ml of catalyst) at a temperature increasing from 400 to 500°. Regeneration can be repeated many times: there was no lowering of catalyst activity observable after 40 regenerations.

Isomerization of chloronaphthalene on aluminosilicate catalyst is completely inhibited by ammonia introduced into the catalyst area. Thus the catalyzate obtained by passage of 4.2 g of 1-chloronaphthalene at 400° over 40 ml of catalyst for 15 minutes with a simultaneous passage rate of 30 ml per minute for ammonia, did not freeze at −15°.

Isomerization of 1-Chloronaphthalene on Aluminum Oxide in the Presence of a Stream of Hydrogen Chloride.

Effect of the isomerization temperature was determined during passage of 8 g per hour of chloronaphthalene on 50 ml of aluminum oxide and 70 - 80 ml per minute hydrogen chloride (mole ratio $C_{10}H_7Cl$:HCl = 1:4). The duration of each experiment was 5 hours (Table 4). With respect to the fact that optimal isomerization temperature is 330-350°, experiments were set up to study the effect of contact time on the extent of isomerization at 330°. A ratio of $C_{10}H_7Cl$: HCl was maintained equal to 1:3. The amount of catalyst was 50.ml. . Experiment time was 5 hours (Table 5).

TABLE 4

Temperature of experiment	300°	330	350	400
Solidification temperature of catalyzate	10.0°	21.0	21.5	17.0
Content of 2-chloronaphthalene (in %)	42.5°	53.0	52.5	48.5

TABLE 5

1-chloronaphthalene feed (in g per hour)	10.0	13.0	16.2	18.0	20.0
Solidification temperature of catalyzate	18°	19	19	17.5	11

The effect of 1-chloronaphthalene and hydrogen chloride ratio was studied at 400°. The quantity of reactants fed, and the catalyst volume, were varied in order to maintain contact time constant. Experiment time was 3 hours. Conditions and experimental results are given in Table 6.

The optimal ratio was subsequently found to be 1:3.

A study of the dynamics of change in activity of aluminum oxide in the isomerization process indicated that a very important effect upon the character of this change is shown upon treating the catalyst with hydrogen chloride.

There is given in Table 7 the effect of preliminary catalyst treatment with hydrogen chloride upon the

activity at the experimental temperature of 350°. Feed amounted to 16.2 g of $C_{10}H_7Cl$ per hour. Mole ratio was $C_{10}H_7Cl:HCl = 1:3$.

TABLE 6

Quantity of catalyst	$C_{10}H_7Cl$ feed (in g/hour)	HCl feed (ml per minute)	Mole ratio of $C_{10}H_7Cl:HCl$	Solidification temperature of catalyzate
30	24	60	1:1	− 3°
37.5	7.8	36	1:2	+ 17
50	7.8	53	1:3	+ 20
80	7.8	95	1:5	+ 18
80	4.0	100	1:10	+ 17

Decrease of aluminum oxide activity is related to its carbonization. Analysis of the aluminum oxide which was worked for 7 hours, indicated 5.58% carbon content. After regeneration under the above-indicated conditions, and treating with hydrogen chloride, the activity of aluminum oxide was regenerated again.

In connection with the fact that only up to 25% 2-chloronaphthalene in terms of catalyzate weight separated upon freezing the catalyzate, while over half of the 2-chloronaphthalene contained in the catalyzate remained in solution form with 1-chloronaphthalene, making it difficult to separate, it appeared an interesting step to increase yield by subjecting the mother liquor from 2-chloronaphthalene to direct isomerization again. As was to be expected, the isomerization processes in mother liquor (mixture of 2-chloronaphthalene with 1-chloronaphthalene containing for example 40% 2-chloronaphthalene) proceeded in a manner identical with that for fresh 1-chloronaphthalene. Solidification temperature for the catalyzate was the same (19 - 20° with 3 hours of work). Thus, by separating the 2-chloronaphthalene crystallizing out and returning the mother liquor to the process, it is possible to convert almost all of the 1-chloronaphthalene into its isomer. The yield of catalyzate during prolonged experiments amounted to 94 - 98% of the 1-chloronaphthalene passed through, the yield of isolated 2-chloronaphthalene being up to 100 g per liter of catalyst within 1 hour of work.

TABLE 7

Catalyst treatment time with HCl	Solidification temperature of the catalyzate obtained, within						
	1st hour	2nd hour	3rd hour	4th hour	5th hour	6th hour	7th hour
Without treatment	− 15°	+ 12.8°	+17.2°	+ 17.4°	+ 14.2°	+ 14.0°	+13.4°
1.5 hours	+ 22.4	+ 21.8	+21.8	+ 21.2	+ 19.6	+ 18.2	+18.2

Solidification temperature of the catalyzate obtained within the first hour of work fluctuated within a range of several degrees. The maximum temperature for catalyzate solidification, obtained at 350° reached 23.8°.

Isomerization of 2-Chloronaphthalene.

2-Chloronaphthalene was used as the starting material, obtained by isomerization of 1-chloronaphthalene with subsequent recrystallization from alcohol. To feed in the 2-chloronaphthalene (m.p. 56 - 57°) the standard buret was replaced by a buret with jacket in which water circulated, preheated to 80°. Isomerization of the 2-chloronaphthalene was carried out at 300, 350, 400 and 450° on 80 ml of aluminosilicate catalyst in a stream of hydrogen chloride. Regeneration of catalyst was carried out between experiments by the above-indicated method.

The catalyzate was frozen out at −10°, and the 2-chloronaphthalene which separated was filtered off. The filtrate from 2-chloronaphthalene upon distillation distilled completely in the range 240 - 262°.

Found %: C 73.27, 73.55; H 4.77, 4.82. $C_{10}H_7Cl$. Calculated %: C 73.86; H 4.34.

Analysis, and the boiling temperature of the filtrate indicated that it (and hence the catalyzate as well) consisted only of a mixture of the chloronaphthalene isomers. This made it possible to determine the composition of catalyzate from a curve for the solidification temperatures for 1- and 2-chloronaphthalene mixtures. Experimental results are given in Table 8. (see next page)

SUMMARY

1. It has been established that 1-chloronaphthalene isomerizes smoothly into 2-chloronaphthalene upon passage of vapors of the former over aluminosilicate catalyst, or aluminum oxide, along with hydrogen chloride.

2. The isomerization reaction is reversible. Under the same conditions, 2-chloronaphthalene isomerizes into 1-chloronaphthalene. Mixtures of isomers containing about 55% of the 2-chloronaphthalene constitute the equilibrium at 350°.

TABLE 8

Isomerization temperature	2-Chloronaphthalene feed (in g per hour)	Mole ratio of $C_{10}H_7Cl:HCl$	Solidification temperature of the catalyzate within the			Content of 2-chloronaphthalene in catalyzate (in %)
			1st hour	2nd hour	3rd hour	
300*	6.20	1:3	23.4*	–	–	55.0
300	11.50	1:3	27.6	–	–	59.0
350	6.25	1:3	–	23.6°*	–	55.0
350	6.50	1:5	20.0	–	–	54.5
400	7.10	1:4	21.6	–	–	53.5
400	11.80	1:3.5	23.0	25.4	26.0°	–
450	6.10	1:5	22.2	–	–	54.0
450	17.85	1:3	23.8	–	–	55.5

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MECHANISM OF ACTION OF ALUMINUM CHLORIDE CATALYSIS

III. KINETICS OF THE BENZENE ALKYLATION REACTION

N. N. Lebedev

In the preceding articles [1,2] the structure of complex aluminum halide compounds with alkyl halides, chloroanhydrides and ketones was investigated. The question of role of these complexes has resulted in conflicting opinions for a long time. Some consider them to be essential intermediates, without which reaction is unable to proceed; others consider these complexes to be catalytic poisons which lower the activity of aluminum chloride. The author has used the kinetic method of investigation to clarify the role of these complexes, and other problems as well, which are related to an explanation for the mechanism of action of aluminum chloride catalysis.

Steele [3], using the reaction of benzyl chloride with toluene, studied for the first time the kinetics of alkylation of aromatic hydrocarbons by means of metallic halides. Due to heterogenity of the catalyst, he was unable to obtain satisfactory results. Later, Uhlich and Hayne [4] studied the kinetics of reaction for propyl chloride with benzene in the presence of gallium chloride, the results of which can hardly be extended to include the aluminum chloride reaction, since the authors used another catalyst.

Questions of the effect of structure upon the reactivity of halogen derivatives and aromatic compounds, as well as influence of the medium and other other factors, have remained in these works obscure.

EXPERIMENTAL

The most suitable solvent was found to be nitrobenzene, which dissolves aluminum chloride, readily, and does not deprive it of its catalytic activity. The author purified nitrobenzene by distillation at atmospheric pressure, and sampling of the middle fraction, freezing out, and finally a vacuum distillation, with sampling of the middle fraction only.

A 10 % solution of sublimed aluminum chloride in nitrobenzene was prepared, by varying the dosage of which, the necessary concentration of catalyst in the reaction mixture was obtained.

Benzene was also purified by boiling with aluminum chloride and distilling on a fractionating column, drying finally with metallic sodium.

Cyclohexyl chloride was selected as the alkyl halide due to its low volatility and relative stability with respect to the action of aluminum chloride. Cyclohexyl chloride, prepared by heating one part of cyclohexanol and 4 parts of hydrochloric acid, was thoroughly purified by concentrated sulfuric acid, washed with water, and then sodium carbonate; after drying with calcium chloride and distilling, it had d_4^{20} 0.9760 and n_D^{20} 1.4612.

The method of observation of reaction course was found to be most difficult during study of the kinetics of the alkylation reaction. The only possibility of observation is apparently the evolution of hydrogen chloride. Steele [3] blew it out with a stream of dry hydrogen, having constructed beforehand an empirical curve for blowing out, from which results were calculated. Uhlich and Hayne [4] determined the volume of evolving gas, disregarding solubility of the hydrogen chloride in reaction medium. The latter method seemed to be less accurate, and the author selected the procedure of blowing out hydrogen chloride with a stream of nitrogen, modifying considerably, however, the technique of calculation.

Reaction by the author was carried out in a 60 ml flask with fused-in bubbler for nitrogen and a gas outlet tube. Charging of reactants was carried out through a neck with ground stopper. Nitrogen from the tank was dried with sulfuric acid and solid alkali and its flow rate determined by a rheometer. To avoid carrying solvent away from the reaction mixture, the nitrogen was then passed through a flask containing a mixture of nitrobenzene and benzene, identical in composition with that of the mixture present in the reaction flask. The flask and reaction flask were placed in a thermostat, where the required temperature was maintained within an accuracy of $\pm$ 0.05°. Nitrogen, together with hydrogen chloride, was passed into an absorber of distilled water, where the hydrogen

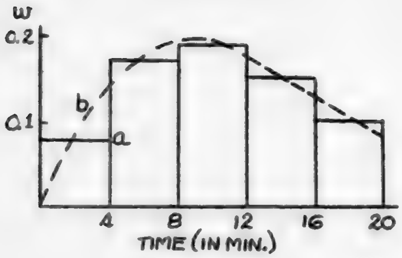


Fig. 1. Relationship of HCl Blow-Out Rate with Time. Explanation in Text

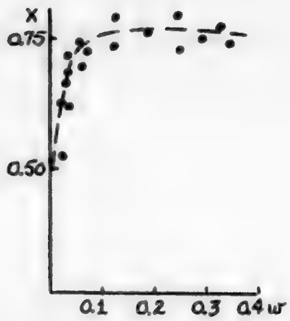


Fig. 2. Relationship between Saturation Coefficient (x) and Rate of Blow-Out (W)

chloride was absorbed. By means of a three-way stopcock it was possible, after a measured time interval determined by a second watch, to pass the gases into another absorber. Titration of the solutions from the absorbing vessels with 0.1 N-NaOH gave the amount of hydrogen chloride evolved during a defined time interval for the reaction.

If n_z = total amount of hydrogen chloride absorbed in the absorber, then the amount of hydrogen chloride formed will be greater in amount than was contained in the gas space of the flask and dissolved in the reaction mixture:

$$\Sigma n = n_z + n_{gas} + n_{dissolved}$$

For the most accurate determination of hydrogen chloride concentration in the gaseous phase, a diagram was constructed (a) according to the experimental data with the coordinates: time of blow-out of hydrogen chloride (W) versus Time (Fig. 1). On the basis of this diagram a curve was then plotted for the true rates of blow-out (b). Using as symbols V = total volume of gases/minute, K = coefficient of solubility for hydrogen chloride, $\underline{x}$ = degree of saturation during bubbling, and taking into account that the volume of gas phase amounted to 40 ml, and the reaction volume 20 ml, we then have

$$\Sigma n = n_z + \frac{W \cdot 40}{V} + \frac{W \cdot K \cdot 20}{V \cdot x} = n_z + \frac{W}{V}\left(40 + \frac{20K}{x}\right).$$

The total volume of gases in its turn is composed of rates for nitrogen, hydrogen chloride, and carrying away of benzene vapors.

Hydrogen chloride solubility coefficients in benzene and nitrobenzene as determined specially by the authors, are given in Table 1 (concentration in the gas and in the liquid phases given in moles/liter.

TABLE 1
Solubility Coefficients of Hydrogen Chloride

Solvent	Temperature			
	20°	30°	40°	50°
Nitrobenzene	16.4	13.7	11.4	9.5
Benzene	11.5	9.3	7.5	6.0

The solubility of hydrogen chloride in benzene-nitrobenzene mixture was calculated according to the principle of additivity.

The saturation coefficient, $\underline{x}$, was determined by special experiments in which hydrogen chloride was blown through a solution of benzene and nitrobenzene. The value was found to depend upon the hydrogen chloride concentration, as indicated in Fig. 2, where blowing rates in millimoles/min. were plotted on the abscissa axis and the saturation coefficient, $\underline{x}$, on the ordinate axis.

Due to the low moisture in starting products while blowing out the reaction mixture, which did not contain cyclohexyl chloride, some hydrogen chloride was evolved; in the experimental results, therefore, a correction was introduced by subtracting from the titration data the values resulting from the blank experiment carried out under the same conditions, but without cyclohexyl chloride.

Confirmatory experiments carried out by the authors with various volumes of reaction mass and nitrogen flow rates, gave deviations from the rate constants averaging in the range of $\pm 2\%$, which indicated sufficient accuracy for the procedure and technique of calculation as developed by the author.

The rate constants (concentrations in m/l, time in min.) which are quoted farther on, are average values for not less than 3 experiments, calculating by the graphic procedure.

Before starting experiments, the author made certain that cyclohexyl chloride in nitrobenzene solution is sufficiently stable with respect to the action of aluminum chloride up to 50°, and that hydrogen chloride is not split out under these conditions. Thus, only an alkylation reaction is possible:

$$C_6H_{11}Cl + C_6H_6 \xrightarrow{AlCl_3} C_6H_5C_6H_{11} + HCl.$$

As has been indicated by Kursanov [5], Mayes and Turner [6], cyclohexylbenzene results in good yield, in this reaction, which makes it quite suitable for study of the kinetics. In order to avoid dealkylation, not less than 7-fold excess of benzene was used everywhere.

The Effect of Alkyl Halide Concentration. In this series of experiments, only the initial concentration of cyclohexyl chloride was varied, all other factors remaining constant (temperature 40°, $AlCl_3$ concentration 0.1 M//liter). The results obtained are given in Table 2.

TABLE 2

Composition of the reaction medium (in volume %)		Initial concentration of cyclohexyl chloride (in M/l).	Rate constant, K_1	Time for half-decomposition (in min.)
Benzene	Nitrobenzene			
75.0	23.7	0.100	0.0190	36.5
75.0	22.5	0.200	0.0194	35.7
75.0	21.5	0.300	0.0195	35.5
12.5	86.2	0.100	0.128	5.4
12.5	85.0	0.200	0.132	5.25
12.5	84.0	0.300	0.131	5.3

With variation in initial concentration of cyclohexyl chloride, the time interval remained almost constant in which the half-reacted (cyclohexyl chloride), and the results of each individual experiment are superimposed well upon a straight line for log C versus time. All of these facts indicated that there was monomolecularity of the alkylation reaction in relation to concentration of alkyl halide:

$$v = k_1[RCl].$$

These data also make it possible to conclude that hydrogen chloride has no effect of any kind upon the reaction rate.

Effect of Benzene Concentration. The difficulty in studying effects of benzene concentration stems from the large effect of medium upon reaction rate, as can be seen from the preceding table. At the same time, the necessity for maintaining excess benzene in the alkylation reaction makes the components of the solvent of importance. In order to maintain the same approximate concentration of medium, and yet modify the benzene concentration, a portion of the latter was replaced by decalin . In the first three experiments of Table 3, this replacement was carried out in such a manner that the volumetric concentration of nitrobenzene remained constant, and in the last three experiments, its molar concentration remained constant.

TABLE 3
The Concentration of $AlCl_3$ was 0.100 m/liter, and of Cyclohexyl Chloride 0.2 m/liter, Temperature 40°.

Experiment No.	Composition of medium (in volume %)			Concentration of benzene (in m/liter)	Rate constant	
	Benzene	Decalin	Nitrobenzene		k_1	k_2
1	25.0	–	72.5	2.81	0.147	0.052
2	12.5	12.5	72.5	1.41	0.0789	0.056
3	6.25	18.75	72.5	0.70	0.0440	0.063
4	25.0	–	72.5	2.81	0.145	0.052
5	12.5	18.0	67.0	1.41	0.0660	0.047
6	6.25	27.0	64.25	0.70	0.0306	0.044

Increase in the k_2 constants is explainable in the first instance by an increase in the molar quantity of nitrobenzene upon replacing benzene with decalin and their decrease in the second series by the high inertness of decalin as a solvent, compared to benzene.

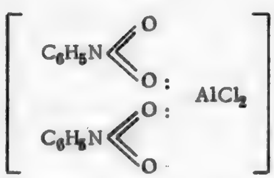
nitrobenzene, with a polar structure [2]. The high thermal dissolution effect of aluminum chloride in nitrobenzene (12200 cal/mole) [7] excludes the possibility of free aluminum chloride being present which is not bound up with the complex. Its solutions in nitrobenzene possess an electroconductivity [8] due to dissociation of the complex into ions [2]:

TABLE 5

Composition of medium (in volume %)		$AlCl_3$ concentration (m/liter)	Temperature	Rate constant K_1	Activation energy (cal/mole)
benzene	nitrobenzene				
12.5	85.0	0.203	20.0°	0.0205	18700
		0.203	30.0	0.0635	
		0.100	30.0	0.0476	
		0.100	40.0	0.130	
		0.025	40.0	0.0520	
		0.025	50.0	0.122	
75.0	22.5	0.203	30.0	0.0217	17500
		0.203	40.0	0.0550	
		0.100	40.0	0.0193	
		0.100	50.0	0.0450	

TABLE 6

Composition of medium (in volume %)		Temperature	Concentration of $AlCl_3$ (m/liter)	Rate constant K_1	Order of reaction, n
benzene	nitrobenzene				
12.5	85.0	30.0°	0.025	0.0200	0.64
12.5	85.0	30.0	0.049	0.0308	0.59
12.5	85.0	30.0	0.100	0.0470	0.44
12.5	85.0	30.0	0.203	0.0642	0.35
12.5	85.0	30.0	0.410	0.0820	
50.0	47.5	40.0	0.049	0.0327	1.05
50.0	47.5	40.0	0.100	0.0690	1.05
50.0	47.5	40.0	0.203	0.146	
75.0	22.5	40.0	0.100	0.0196	1.44
75.0	22.5	40.0	0.203	0.0550	
75.0	22.5	50.0	0.100	0.450	1.46
75.0	22.5	50.0	0.203	0.125	



$$[AlCl_4] \rightleftharpoons [(C_6H_5NO_2)_2AlCl_2]^+ + [AlCl_4]^- .$$

A fractional order of reaction with respect to aluminum chloride in nitrobenzene medium indicates that the actual catalyst in this case is one of the products of complex dissociation. Inasmuch as the constant for this dissociationa is small [8], the extent of dissociation therefore is

$$\alpha = \frac{-K + \sqrt{K^2 + 4Kc}}{2c} \approx \sqrt{\frac{K}{c_{AlCl_3}}}$$

and the rate equation takes the form of

$$v = k'\alpha c_{AlCl_3}[RCl][C_6H_6] = kc^{0.5}_{AlCl_3}[RCl][C_6H_6],$$

which is indeed observed in the reaction course carried out in nitrobenzene.

Ionic character of the catalysis is confirmed by the strong influence of medium upon the rate of this reaction, and in the well-ionizing solvent (nitrobenzene) it proceeds more rapidly than in benzene.

Of the two dissociation products being formed, the true catalyst for the process can only be the cation, inasmuch as the anion $(AlCl_4)^-$ is found in all complexes of aluminum chloride, also catalytically inactive (for example its complexes with ketones).

Upon changing the medium and moving to poorly-ionizing solvents, the cation concentration is strongly decreased due to weak dissociation of the complex. Instead of a rapid catalysis proceeding with the cation, there is a slow reaction in which the role of active reagent is played by the undissociated molecules of catalyst.

The general kinetic equation in such a case will be as follows:

$$\nu = k_i ([AlCl_3]^{0.5} + k_s [AlCl_3]^2) [RCl] [C_6H_6],$$

where k_i = constant for the rapid reaction rate of ionic catalysis, k_s = rate constant for slow reaction of a bimolecular catalysis.

Superimposition of both mechanisms in various ratios with respect to properties of the medium results in an intermediate value for the order of reaction for aluminum chloride.

SUMMARY

1. A procedure has been developed and the kinetics studied for the reaction of cyclohexyl chloride with benzene in the presence of aluminum chloride and in mixtures of benzene and nitrobenzene.

2. The reaction has been found to be monomolecular with respect to alkyl halide and benzene, but has an intermediate value from 0.5 to 2nd order for aluminum chloride, depending upon the composition of the medium.

3. Activation energies for the reaction have been determined.

4. A strong effect of medium upon the reaction rate has been observed.

5. The results obtained are interpreted by the existence of two mechanisms for the process — a rapid reaction of ionic catalysis in highly ionizing solvent, and a slow reaction of bimolecular catalysis in weakly ionizing medium.

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* See Consultants Bureau Translation, page 1975.

BEHAVIOR OF N-(β-HYDROXYETHYL)-ANILINE AND N-(β-HYDROXYETHYL)-o-TOLUIDINE IN THE PRESENCE OF ALUMINOSILICATE

Yu. K. Yuryev and L. F. Gorin

The synthesis of compounds of the indole and dihydroindole series from the readily available N-(β-hydroxyethyl)-arylamines is of great interest.

According to the data of Knorr [1], only an insignificant quantity of indole could be isolated in experiments involving the closure of the ring in N-(β-hydroxyethyl)-aniline with the aid of various condensing agents. Alkaline fusion [2] at 240-280° in a reducing atmosphere led to the splitting off of two hydrogen molecules and to the formation of indoxyl in a yield of 60%. Upon heating with phosphorus pentoxide in xylene [3], N,N'-diphenylpiperazine was obtained together with an insignificant quantity of a fraction with a b.p. of 220-270° which, in the opinion of the authors, contained dihydroindole.

Shorygin and Belov [4] described a series of experiments involving the dehydration of N-(β-hydroxyethyl)-aniline. When conducted over Glukhov clay at 450-520°, N-(β-hydroxyethyl)-aniline yielded a viscous yellow catalyzate from which only a small quantity of aniline could be distilled off; upon heating with anhydrous oxalic acid, it did not change; it resinified under the action of aluminum chloride; it yielded the dimer of N-vinylaniline upon heating 2-3 hours with sodium to 260-280°.

Yuryev and Novitsky [5] obtained N,N'-diphenylpiperazine by heating N-(β-hydroxyethyl)-aniline with an aluminosilicate cracking catalyst at 240°.

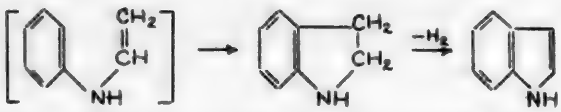
In the present work the possibility of obtaining indole and dihydroindole from N-(β-hydroxyethyl)-aniline in the presence of the same catalyst, but at a much higher temperature, was studied. It was established that at 300° the dehydration of N-(β-hydroxyethyl)-aniline does not proceed simply, but is complicated by dehydrogenation, hydrogenation and alkylation of the reaction products. The following were isolated from the mixture of reaction products: aniline (chief reaction product), 4-ethylaniline, indole, skatole and diphenylpiperazine. It was shown by the preparation of crystalline derivatives that p-toluidine, N-ethylaniline, dihydroindole, 2,4-diethylaniline and quinaldine were also contained in the reaction products. Finally, we isolated a mixture of alkylindoles with a b.p. of 112-124° (4 mm), in which the presence of diethyl- and triethylindoles, the structures of which were not established, was proved by preparing the picrates. It should be noted that no appreciable evolution of gas or formation of low-boiling reaction products was observed.

The results obtained in the present work make it possible to express the following considerations concerning the mechanism of the reaction studied by us. As was indicated above, the dehydration of N-(β-hydroxyethyl)-aniline, in the presence of aluminosilicate at 240° [5], leads to the formation of N,N'-diphenylpiperazine, while when the temperature was raised to 300°, it was possible to isolate only an insignificant quantity of the latter (2%).

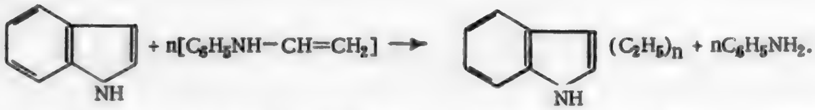
Topchieva and Yun-Pin [6] showed for the first time that ethyl alcohol yields diethyl ether in the presence of aluminosilicate at 250°, while at 300-320°, the chief reaction product is ethylene. At 300-320°, diethyl ether is also dehydrated with the formation of ethylene. We assume that the dehydration of N-(β-hydroxyethyl)-aniline also proceeds according to an analogous scheme; the product of its dehydration over aluminosilicate at 300° should consequently be the unstable N-vinylaniline: $C_6H_5NHCH_2CH_2OH \rightarrow [C_6H_5NHCH{=}CH_2] + H_2O$. The formation of the latter can also be represented as a result of the cleavage of N,N'-diphenylpiperazine:

N-Vinylaniline undergoes the following further series of reactions:

1. Intramolecular alkylation with the formation of dihydroindole which loses hydrogen to yield indole:



A mixture of alkylindoles and aniline was obtained as a result of the further alkylation of indole with vinylaniline with subsequent hydrolysis, cleavage of water from the ethanolindoles formed and addition of hydrogen to vinylindole:



2. Alkylation of aniline with subsequent hydrolysis of the alkylation product, cleavage of water from the formed 4-(β-hydroxyethyl)-aniline, and addition of hydrogen to 4-vinylaniline led to the formation of 4-ethylaniline:

$$C_6H_5NH_2 + [C_6H_5NH-CH=CH_2] \longrightarrow [C_6H_5NH-CH_2-CH_2-C_6H_4NH_2] \xrightarrow{+\,HOH} \left[C_6H_4\begin{matrix} NH_2 \\ CH_2CH_2OH \end{matrix}\right] +$$

$$+\, C_6H_5NH_2 \xrightarrow{-\,HOH} \left[C_6H_4\begin{matrix} NH_2 \\ CH=CH_2 \end{matrix}\right] \xrightarrow{+H_2} C_6H_4\begin{matrix} NH_2 \\ CH_2CH_3 \end{matrix}$$

2,4-diethylaniline was obtained by the further alkylation of 4-ethylaniline.

3. Addition of hydrogen with the formation of N-ethylaniline:

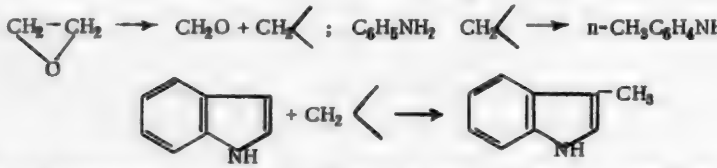
$$[C_6H_5NH-CH=CH_2] \xrightarrow{+H_2} C_6H_5NHC_2H_5.$$

4. Isomerization into acetanil and formation of N-ethylaniline from it as a result of the addition of hydrogen:

$$[C_6H_5NH-CH=CH_2] \longrightarrow [C_6H_5N=CH-CH_3] \xrightarrow{+\,H_2} C_6H_5NHC_2H_5.$$

Along with these processes, there no doubt occurs the decomposition of N-(β-hydroxyethyl)-aniline into aniline and ethylene oxide which isomerizes into acetaldehyde; the latter condenses with aniline to form quinaldine.

The mechanism of formation of p-toluidine and skatole is not clear. If, however, it is assumed that the decomposition of ethylene oxide into formaldehyde and the methyl radical [7] is possible only to an insignificant extent, then the formation of insignificant quantities of p-toluidine and skatole can be represented as the result of the alkylation of aniline and, respectively, indole with the methyl radical [8].



N-(β-Hydroxyethyl)-o-toluidine behaves similarly under analogous conditions. o-Toluidine (the chief reaction product), 2-methyl-4-ethylaniline and 7-methylindole were isolated from the complex mixture of reaction products.

We consider the formation of 7-methylindole in the absence of tetrahydroquinoline or quinoline in the reaction products as a confirmation of the mechanism which we proposed for the dehydration of N-(β-hydroxyethyl)-aniline.

EXPERIMENTAL

Dehydration of N-(β-Hydroxyethyl)-aniline.

N-(β-Hydroxyethyl)-aniline (b.p. 176° at 19 mm; n_D^{20} 1.5763; d_4^{20} 1.0945) [9] was conducted in a stream

of nitrogen over aluminosilicate cracking catalyst at 300° at a volumetric rate of 0.5 ml/ml of catalyst per hour. About 30 g of material was introduced in each experiment, after which the catalyst was regenerated [10]. 253 g of catalyzate (of which 40 g was water) was obtained from 300 g of N-(β-hydroxyethyl)-aniline.

The following fractions were isolated by two-fold fractionation of the oily portion of the catalyzate (dried with calcined potash) in a vacuum at 5 mm from a flask with a fractionating column: 1st b.p. 60-61.5°, 135.5 g; 2nd, b.p. 61.5-85°, 6.9 g; 3rd, b.p. 85-118°, 18.4 g; 4th b.p. 118-155°, 33.4 g; 5th, b.p. 155-186°, 4.0 g; residue 11.5 g.

Crystals precipitated from the 5th fraction and from the residue, and their quantity was increased by freezing out. After having been filtered off, washed with ether and recrystallized from alcohol, they melted at 163° and consisted of N,N'-diphenylpiperazine (5.5 g); a mixed sample with known diphenylpiperazine displayed no melting point depression.

The picrate (from alcohol) consisted of yellow needles with an m.p. of 172-173°; a mixed sample with the known picrate of N,N'-diphenylpiperazine displayed no melting point depression.

The literature data for N,N'-diphenylpiperazine are: m.p. 163° [5]; m.p. 163-164° [11]; m.p. 163.5-164.5° [12]; picrate: m.p. 172-173° [5].

Fractions Nos. 1,2,3 and 4 were fractionated twice more in a vacuum at 10 mm in a column with an efficiency of 18 theoretical plates. The results obtained in the second fractionation with the column, are presented in Table 1.

TABLE 1

Fraction No.	B.p. at 10 mm	Quantity (in g)	n_D^{20}	d_4^{20}	Fraction No.	B.p. at 10 mm	Quantity (in g)	n_D^{20}	d_4^{20}
1	69.0 - 69.5°	133.5	1.5853	1.0221	11	100.0 - 111.5°	0.58	1.5683	–
2	69.5 - 76.0	1.7	1.5846	–	12	111.5 - 117.5	0.7	1.5801	–
3	76.0 - 80.0	0.9	1.5778	–	13	117.5 - 119.5	1.9	1.6014	1.0590
4	80.0 - 81.5	1.1	1.5645	0.9831	14	119.5 - 127.5	2.2	1.6032	–
5	81.5 - 85.5	0.9	1.5618	–	15	127.5 - 130.0	2.1	1.6078	–
6	85.5 - 90.0	0.2	1.5610	–	16	130.0 - 136.5	3.6	1.5943	–
7	90.0 - 92.5	0.9	1.5565	–	17	136.5 - 146.0	3.7	1.5913	–
8	92.5 - 93.0	1.7	1.5558	0.9680	18	146.0 - 148.5	6.9	1.5870	–
9	93.0 - 96.0	0.9	1.5575	–	19	148.5 - 152.0	2.6	1.5895	–
10	96.0 - 100.0	0.6	1.5603	–	Residue	....	15.9	–	–

a) Aniline. Fractions Nos. 1 and 2 consisted of aniline. The yield was 135.2 g (65.5%). The acetanilide obtained from them melted at 115°, and a mixed sample with known acetanilide displayed no melting point depression.

b) p-Toluidine. The bulk of Fraction No. 4 consisted of p-toluidine. The N-acetyl-p-toluidine (0.6 g) obtained from it melted at 145.0-146.0° after recrystallization from alcohol; a mixed sample with known N-acetyl-p-toluidine displayed no melting point depression. The picrate (from benzene) melted at 180°; a mixed sample with the known picrate of p-toluidine displayed no melting point depression.

The literature data for p-toluidine are: b.p. 82.2° (10 mm), m.p. 45° [13]; N-acetyl-p-toluidine; m.p. 145.5 [14]; p-toluidine picrate: m.p. 180° (with decomposition) [15].

c) N-ethylaniline: 0.8 g of Fraction No. 5 was stirred with 0.6 ml of concentrated hydrochloric acid [16]. The hydrochloride crystals which were formed were filtered off and washed with concentrated hydrochloric acid. After recrystallization from alcohol the hydrochloride melted at 176°, and a mixed sample with the known hydrochloride of N-ethylaniline displayed no melting point depression.

Found %: N 8.71, 8.89. $C_8H_{12}NCl$. Calculated %: N 8.89.

Literature data for N-ethylaniline hydrochloride: m.p. 176° [17].

d) 4-Ethylaniline: Fraction No. 8 with a b.p. of 92.5 - 93° (10 mm), n_D^{20} 1.5558; d_4^{20} 0.9680; MR 40.21;

calculated 38.96, consisted of 4-ethylaniline.

Found %: C 79.27, 79.52; H 9.05, 8.98; N 11.19, 11.26. $C_8H_{11}N$. Calculated %: C 79.30; H 9.15; N 11.56.

After recrystallization from water, the 4-ethylacetanilide (0.4 g) [18] melted at 94°.

Found %: N 8.78. $C_{10}H_{13}ON$. Calculated %: N 9.15.

4-Ethylaniline picrate (from benzene) melted at 168°.

Found %: N 16.24, 16.10. $C_{14}H_{14}O_7N_4$. Calculated %: N 15.99.

The 4-ethylaniline sulfate (0.8 g) obtained by mixing 2 N sulfuric acid with a solution of 0.5 g of Fraction No. 8 in 0.8 ml of alcohol, and dilution with water until the solution became turbid [19], melted at 239° after recrystallization from hot water.

Found %: H_2SO_4 27.13, 27.12 (by titration with phenolphthalein as indicator). $C_{16}H_{22}N_2 \cdot H_2SO_4$. Calculated %: H_2SO_4 27.14.

Literature data for 4-ethylaniline: b.p. 213-214°; n_D^{22} 1.5529; d_4^{22} 0.975 [20]; b.p. 93.8° (10 mm) [13]; 4-ethylacetanilide: m.p. 95° [21]; 4-ethylaniline sulfate: m.p. 239° [19].

Fractions Nos. 11-19 gave a positive reaction for indole (pine shavings, moistened with hydrochloric acid, became red colored).

To isolate indole and determine the composition of Fractions Nos. 10-15, on the basis of their solubility in ether, these fractions were subjected to fractional precipitation in ethereal solution by picric acid. After the slightly ether-soluble yellow picrates had been precipitated, the ethereal solution was red-colored due to the readily soluble indole picrate [22]. The picrates with an identical melting point, obtained from a given fraction, were combined. The identity of picrates with identical melting points but obtained from different fractions, was established by a mixed melting point test.

The results of the fractional precipitation of the picrates are presented in Table 2.

e) Dihydroindole: The picrates of Nos. 4, 5, 8, and 11 consisted of dihydroindole picrate. A mixed sample of these picrates displayed no melting point depression: m.p. 173-174° (0.3 g).

Found %: N 16.13, 16.06. $C_{14}H_{12}O_7N_4$. Calculated %: N 16.16.

On adding an alcoholic solution of oxalic acid to 0.2 g of Fraction No. 12, white, thread-like crystals of dihydroindole oxalate were obtained which melted at 127-128° after recrystallization from aqueous alcohol. Upon being heated in 96% alcohol, they were converted into the neutral oxalate, which crystallized with three molecules of water.

5.180 mg substance: 0.330 ml N_2 (23°, 748 mm). Found %: N 7.23. $C_{18}H_{16}O_2N_2 \cdot 3H_2O$. Calculated %: N 7.34.

Literature data for dihydroindole: b.p. 228-231°; n_D^{25} 1.5891 [23]; b.p. 100-101° (12 mm) [22]; dihydroindole picrate: m.p. 174° [23]; acid oxalate of dihydroindole: m.p. 127-128° [24].

f) 2,4-Diethylaniline: A mixed sample of the picrates of Nos. 6, 9, and 13 displayed no melting point depression. In all, 2.1 g of a picrate with a m.p. of 184° was obtained. The picrate was decomposed with ammonia and the bases extracted with ether. The ethereal extract was washed with water and dried by fusing with sodium hydroxide. After distilling off the ether and fractionally distilling the residue, 0.5 g of an oil was obtained which consisted of 2,4-diethylaniline. 2,4-Diethylacetanilide was obtained by heating 0.2 g of the oil with 0.2 g of glacial acetic acid [25]; after recrystallization from alcohol and vacuum sublimation, it melted at 103-104°.

The benzenesulfonamide of 2,4-diethylaniline was obtained as follows: 0.3 g of the oil was shaken with 0.6 g of benzenesulfochloride. After recrystallization from alcohol, the sulfonamide (soluble in alkali) melted at 112° and consisted of the benzenesulfonamide of 2,4-diethylaniline.

Found %: N 3.75, 3.57. $C_{16}H_{19}O_2NS$. Calculated %: N 3.94.

Literature data for 2,4-diethylaniline: b.p. 140-142° (20 mm); 2,4-diethylacetanilide: m.p. 104° [25].

g) Quinaldine: The picrates of Nos. 16 and 18, with a m.p. of 192°, consisted of quinaldine picrate. A mixed sample with known quinaldine picrate displayed no melting point depression: m.p. 192°.

TABLE 2

Fraction		Picrates obtained				
No.	Quantity (in g)	Picrate No.	M.p. of picrate	Quantity (in g)	M.p. after recrystallization	Designation of the picrate
10	0.6	1	168°	0.9	168°	4-Ethylaniline picrate (a mixed sample with the picrate from Fraction No. 8 displayed no melting point depression)
		2	161	0.4	–	
11	0.5	3	158	0.4	–	[illegible]
		4	167	0.4	173	Dihydroindole picrate
		5	172	0.1	173 - 174	Dihydroindole picrate
12	0.5	6	183	0.3	184	2,4-Diethylaniline picrate
		7	165	0.3	–	–
		8	170	0.2	174	Dihydroindole picrate
13	1.9	9	182	1.6	184	2,4-Diethylaniline picrate
		10	162	0.5	–	–
		11	168	0.2	173 - 174	Dihydroindole picrate
		12	176	0.1	–	–
14	2.2	13	183	0.2	184	2,4-Diethylaniline picrate
		14	171	0.3	–	–
		15	184	0.3	–	–
		16	188	0.4	192	Quinaldine picrate
15	2.1	17	179	0.2	–	–
		18	187	0.3	192	Quinaldine picrate

Found %: N 13.68, 14.59. $C_{16}H_{12}O_7N_4$. Calculated %: N 15.04.

Literature data for quinaldine picrate: m.p. 191-192° [26].

h) Indole: The ethereal solutions, left after precipitating the difficultly ether-soluble picrates from Fractions Nos. 11 - 15, were combined, treated with ammonia solution, diluted with hydrochloric acid and then with soda solution. After drying with calcined potash and distilling off the ether in a vacuum, the residue crystallized. 2.7 g of a substance with an m.p. of 43° was obtained. After recrystallization from n-hexane and vacuum sublimation, the substance melted at 52° and consisted of indole. A mixed sample with known indole displayed no melting point depression. The indole picrate (from benzene) consisted of shiny red needles with an m.p. of 181-182° (upon rapid fusion in bulk); a mixed sample with known indole picrate displayed no melting point depression.

Found %: N 16.15, 16.06. $C_{14}H_{10}O_7N_4$. Calculated %: N 16.19.

Literature data for indole: b.p. 123° (5 mm), m.p. 52° [27]; indole picrate: m.p. 181-182° [28].

i) Skatole: 0.3 g of crystals with an m.p. of 82° were isolated by freezing out from a solution of 3.4 g of Fraction No. 16 (b.p. 130 - 136.5° at 10 mm). After recrystallization from water and vacuum sublimation, the crystals melted at 92 - 93° and consisted of skatole. A mixed sample with known skatole displayed no melting point depression (m.p. 93°).

Found %: N 10.95, 11.15. C_9H_9N. Calculated %: N 10.68.

Skatole picrate (from benzene) melted at 170 - 171° (upon rapid fusion in bulk); a mixed sample with known skatole picrate displayed no melting point depression.

Found %: N 15.49. $C_{15}H_{12}O_7N_4$. Calculated %: N 15.54.

Literature data for skatole: m.p. 95°; skatole picrate: m.p. 170 - 171° [29].

j) Alkylindoles: Fractions Nos. 17, 18, 19 and the residue from the fractional distillation were steam distilled. The initial N-(β-hydroxyethyl)-aniline was not detected in the non-steam-distillable residue. The distillate was extracted with ether; the ethereal extract was repeatedly washed with dilute hydrochloric acid

and water and dried with potash. After distilling off the ether, the residue was vacuum distilled; 15 g of an oil with an indole odor and a b.p. of 112 - 124° (8 mm) was isolated (it gave an indole reaction on pine shavings, moistened with hydrochloric acid) which resinified as a result of the action of concentrated hydrochloric acid and gave a red liquid with nitric acid.

Skatole picrate (0.3 g) with an m.p. of 171° was obtained by fractional precipitation of the picrates from the benzene solution.

After concentration of the filtrate and additionof petroleum ether [30], an orange-red picrate with an m.p. of 143° precipitated from it. The picrate obtained decomposed upon solution in all of the solvents used. Decomposition of the picrate with ammonia, distillation of the base and secondary precipitation gave a picrate with the same melting point.

5.587 mg substance: 0.631 ml N_2 (26°, 747 mm). 5.839 mg substance: 0.650 ml N_2 (23°, 754 mm). Found %: N 12.87, 12.74. $C_{20}H_{22}O_7N_4$. Calculated %: N 13.02.

The analytical data agree with those of triethylindole picrate.

A picrate with an m.p. of 136° was obtained from the filtrate after precipitating the picrate with an m.p. of 143° and after concentration and addition of petroleum ether. Subsequent concentration of the filtrate and repeated precipitation with petroleum ether led to a picrate with an m.p. of 124° (red-brown needles). A second reprecipitation of the picrate did not change its melting point.

5.335 mg substance: 0.649 ml N_2 (26°, 751 mm). 5.013 mg substance: 0.605 ml N_2 (23°, 751 mm). Found %: N 13.72, 13.75. $C_{18}H_{18}O_7N_4$. Calculated %: N 13.93.

The analytical data agree with those for diethylindole picrate.

5 g of a mixture of the ethylindoles was heated for 5 hours with excess acetic anhydride. After distilling off the acetic anhydride and acetic acid, the residue was steam distilled. About 1 g of base distilled off, which was extracted with ether, dried with potash and after distilling off the ether, was vacuum distilled. The picrate, obtained from the benzene solution by precipitation with petroleum ether, melted at 143°. A mixed sample with the previously prepared triethylindole picrate displayed no melting point depression. It can consequently be concluded that one of the radicals in the triethylindole is bound to the nitrogen atom.

Dehydration of N-(β-Hydroxyethyl)-o-toluidine

N-(β-Hydroxyethyl)-o-toluidine [9] (b.p. 146° at 3 mm; n_D^{20} 1.5690; d_4^{20} 1.0794) was conducted over aluminosilicate cracking catalyst under conditions analogous to those described above, i.e., at 300° at a volumetric rate of 0.5 ml/ml of catalyst per hour. 300 g in all of N-(β-hydroxyethyl)-o-toluidine was conducted over the catalyst. No appreciable gas formation was observed. 220 g of catalyzate which contained 27 g of water, was obtained. After separating the water, the catalyzate, dried with calcined potash, was distilled initially from a flask with a fractionating column; no low-boiling substances were detected in the reaction product. By subsequent redistillation at 7 mm, the following fractions were isolated: 1st b.p. 71.5 - 72.5°, 113 g; 2nd b.p. 72.5 - 87°, 14 g; 3rd b.p. 87 - 108°, 4 g; 4th b.p. 108 - 128°, 20 g; 5th b.p. 128 - 140°, 14.6 g; residue 22 g.

Further fractionation with a column with an efficiency of 18 theoretical plates in a vacuum at 7 mm gave the results presented in Table 3.

a) o-Toluidine: Fraction No. 1 (b.p. 71.5 - 72° at 7 mm; n_D^{20} 1.5723; d_4^{20} 0.9978) consisted of o-toluidine. The yield was 112.5 g (54.0 %). The N-acetyl-o-toluidine obtained from it melted at 110°, and a mixed sample with known N-acetyl-o-toluidine displayed no melting point depression.

Literature data for o-toluidine: b.p. 82° (10 mm) [13], b.p. 199.7° (760 mm) [13]; n_D^{20} 1.57276; d_4^{20} 0.9986 [31]; N-acetyl-o-toluidide: m.p. 110° [32].

b) 2-Methyl-4-ethylaniline: Fraction No. 4 (2.3 g; b.p. 106.5 - 107° at 7 mm; n_D^{20} 1.5514; d_4^{20} 0.9644; MR_D 44.74. $C_9H_{13}NF_3$. Calculated: 43.58) consisted of 2-methyl-4-ethylaniline.

Found %: C 80.09, 79.94; H 9.66, 9.53; N 10.39, 10.58. $C_9H_{13}N$. Calculated %: C 80.03; H 9.7; N 10.36.

After recrystallization from dilute alcohol, the acetyl derivative of 2-methyl-4-ethylaniline [21] melted at 105 - 105.5°.

Found %: N 7.86, 7.91. $C_{11}H_{15}ON$. Calculated %: N 7.90.

TABLE 3

Fraction No.	Boiling point	n_D^{20}	d_4^{20}	Quantity (in g)	Fraction No.	Boiling point	n_D^{20}	d_4^{20}	Quantity (in g)
1	71.5 - 72.0°	1.5723	0.9978	112.5	7	126.0 - 129.5°	–	–	4.0
2	72.0 - 97.0	1.5680	–	4.0	8	129.5 - 138.0	1.5976	–	6.5
3	97.0 - 106.5	1.5581	–	5.7	9	138.0 - 140.0	1.5947	1.0315	5.2
4	106.5 - 107.0	1.5514	0.9644	2.3	10	140.0 - 144.5	1.5895	–	1.8
5	107.0 - 108.0	1.5532	–	1.6	11	144.5 - 147.5	1.5860	–	4.0
6	108.0 - 126.0	1.5680	–	3.5	12	147.5 - 149.0	1.5855	–	1.0
					Residue				10.8

The literature data for 2-methyl-4-ethylaniline: b.p. 229 - 230°; melting point of the acetyl derivative 105 - 106° [21].

c) 7-Methylindole: Fraction No. 7 (4 g; b.p. 126 - 129.5° at 7 mm) contained a crystalline substance. After freezing out, filtering and washing with ether, 2.7 g of a substance with an m.p. of 78° was obtained. After recrystallization from water and sublimation, the substance melted at 85° and consisted of 7-methylindole.

Found %: C 82.35, 82.30; H 6.97, 6.89; N 10.48, 10.42. C_9H_9N. Calculated %: C 82.50; H 6.87; N 10.61.

A mixed sample with skatole and with α-methylindole displayed melting point depression: m.p. 75° and 58° respectively. 7-Methylindole picrate (from alcohol) consisted of red needles with a m.p. 176°.

Found %: N 15.73, 15.75. $C_{15}H_{12}O_7N_4$. Calculated %: N 15.54.

Literature data for 7-methylindole: b.p. 266°; m.p. 85°; 7-methylindole picrate: m.p. 176° [33].

SUMMARY

1. The dehydration of N-(β-hydroxyethyl)-aniline and N-(β-hydroxyethyl)-o-toluidine in the presence of aluminosilicate at 300° is complicated by dehydrogenation, hydrogenation and alkylation of the reaction products.

Aniline (the chief reaction product), 4-ethylaniline, indole, skatole and N,N'-diphenylpiperazine were isolated from the mixture of the products of the dehydration of N-(β-hydroxyethyl)-aniline. The presence of p-toluidine, N-ethylaniline, dihydroindole, 2,4-diethylaniline and quinaldine, and also of a mixture of di- and triethylindoles, was demonstrated by the preparation of crystalline derivatives.

2. o-Toluidine (the chief reaction product), 2-methyl-4-ethylaniline, and 7-methylindole were isolated from the product of the dehydration of N-(β-hydroxyethyl)-o-toluidine.

3. A scheme for the mechanism of the formation of the reaction products enumerated above was prepared.

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THE REACTION OF TRIETHYLSILANE WITH AMMONIA AND AMINES

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It was found in 1929 [1] that triphenylsilane reacts with a solution of sodium in liquid ammonia with formation of hexaphenyldisilazane:

$$2(C_6H_5)_3SiH + NaNH_2 \longrightarrow (C_6H_5)_3SiNHSi(C_6H_5)_3 + 2H_2.$$

Kraus and Nelson [2] subsequently found that triethylsilane reacts with an ammoniacal solution of potassium amide according to the scheme:

$$2(C_2H_5)_3SiH + KNH_2 \longrightarrow (C_2H_5)_3SiNKSi(C_2H_5)_3 + 2H_2.$$

Upon treatment with a solution of ammonium bromide in liquid ammonia, the potassium derivative is converted into hexaethyldisilazane.

The reaction of triphenylsilane [1, 3] and triethylsilane [2] with ethylamine in the presence of lithium which proceeds according to the following scheme, is also described in the literature:

$$R_3SiH + C_2H_5NH_2 \xrightarrow{Li} R_3SiNHC_2H_5 + H_2. \; (R = C_6H_5, C_2H_5)$$

Lithium participates as a catalyst in this reaction; the rate of the reaction increases with increase in the concentration of lithium in the solution.

Gilman and co-workers [4] showed that triphenylsilane reacts with lithium dialkylamides according to the scheme:

$$(C_6H_5)_3SiH + LiNR_2 \longrightarrow LiH + (C_6H_5)_3SiNR_2.$$

The reaction of triethylsilane with ammonia and also with aliphatic, alicyclic and aromatic amines, both at ordinary and under increased pressure, was studied in the present work; it was shown under these conditions that triethylsilane reacts with ammonia in the presence of potassium amide even at $-35°$ with the formation of free hexaethyldisilazane, the yield of which amounts to 67 % of the theoretical. At the same time, triethylsilane does not react with ammonia at this temperature in the presence of sodium amide. Neither does triethylsilane react with ammonia in the absence of catalysts in an autoclave at 80 - 90°. The reaction of triethylsilane with ammonia could be brought about in the presence of lithium amide or sodium amide when it was carried out in an autoclave at temperatures of 20° and higher. Thus, for example, triethylsilane and ammonia in the presence of $LiNH_2$ at 20° forms 34% triethylaminosilane and 17% hexaethyldisilazane after 25 hours. In the presence of sodium amide, triethylsilane with ammonia forms 46% triethylaminosilane and 20% hexaethyldisilazane at 70° after 1 hour. It should be noted that sodium amide itself does not react with triethylsilane at 110°.

Thus, the reaction of triethylsilane with ammonia, which is catalyzed by the amides of the alkali metals, proceeds according to the scheme:

$$\begin{aligned} (C_2H_5)_3SiH + NH_3 &\xrightarrow{MNH_2} (C_2H_5)_3SiNH_2 + H_2; \\ (C_2H_5)_3SiH + (C_2H_5)_3SiNH_2 &\longrightarrow (C_2H_5)_3SiNHSi(C_2H_5)_3 + H_2. \end{aligned} \quad (M = K, Na, Li)$$

This scheme explains the increase in the yield of hexaethyldisilazane with increase in the atomic number of the alkali metal which is acting as the catalyst, since under these conditions, the rate of the reaction of triethylsilane with the amines [in the given case $(C_2H_5)_3SiNH_2$] increases. Another possible scheme for the formation of hexaethyldisilazane:

$$2(C_2H_5)_3SiNH_2 \longrightarrow (C_2H_5)_3SiNHSi(C_2H_5)_3 + NH_3.$$

appears to be less probable.

Primary aliphatic amines (ethylamine, n-propylamine) and aniline react smoothly with triethylsilane in the presence of the corresponding alkylamide of potassium, with the formation of triethyl(alkylamino)silanes in yields of 82 - 92%. Thus, for example, upon boiling triethylsilane with n-propylamine in which 2.5 mole%

of potassium is dissolved, when the reagents are taken in a molar ratio of 1:1.7, the theoretical quantity of hydrogen is evolved and 82.5% of triethyl-(n-propylamino)silane is formed. In the analogous reaction of triethylsilane with aniline, the yield of triethyl(phenylamino)silane amounts to 90%. On the other hand, in presence of sodium phenylamide triethylsilane does not react with aniline when boiled.

Primary aliphatic amines with secondary and tertiary alkyl radicals (isopropylamine, tert-butylamine, tert-amylamine, fenchylamine) and secondary aliphatic amines with primary alkyl radicals (diethylamine, di-n-butylamine, diisobutylamine) practically do not react with triethylsilane in the presence of the corresponding potassium amine derivative. However, when the reaction is carried out in an autoclave at 200 - 210°, the indicated amines react smoothly with triethylsilane with the formation of the corresponding triethyl(dialkylamino)silanes. Secondary amines with secondary radicals (dicyclohexylamine) do not react with triethylsilane even on heating for 13 hours in an autoclave at 240°.

The conditions of our experiments in which triethylsilane reacted with ammonia and amines are presented in Table 1. The physical properties of the 12 aminoderivatives of triethylsilane obtained by us, 8 of which were previously unknown, their analytical data and the molecular weight determinations are set forth in Table 2.

All the results obtained in the present work show that the reaction of triethylsilane with ammonia and amines is one of nucleophile substitution (type S_{N_2} of Ingold-Hughes) and can be represented by the following scheme:

$$RNH^- + (C_2H_5)_3SiH \longrightarrow [RNH...(C_2H_5)_3Si...H]^- \xrightarrow{RNH_2} RNHSi(C_2H_5)_3 + H_2 + RNH^-.$$

TABLE 1

Data on the Experiments Involving the Reaction of Triethylsilane with Ammonia and Amines

Initial amine R' =	R''	Catalyst metal	Ratio of reagents: R'R''NH: $(C_2H_5)_3SiH$: M	Temp. of reaction	Duration of reaction (hrs.)	Yield of end products of reaction (in%): Hydrogen	$R_3SiNR'R''$
H	H	–	12: 1	80 - 90°	6	0	0
H	H		15: 1: 0.4	20	20	100	34.3 + 17.1 $(C_2H_5)_3SiNHSi(C_2H_5)_3$
H	H	Na	19: 1: 0.1	– 35 *	6	0	0
H	H	Na	15: 1: 0.04	70	1	100	20.4 + 45.9 $(C_2H_5)_3SiNHSi(C_2H_5)_3$
H	H	K	19: 1: 0.25	–35 *	8	100	66.8 $(C_2H_5)_3SiNHSi(C_2H_5)_3$
H	C_2H_5	K	2: 1: 0.03	80 - 100	2	100	91.2
H	n-C_3H_7	K	1.7: 1: 0.03	180 *	7	100	82.5
H	n-C_3H_7	K	1.7: 1: 0.08	105 *	8	0	0
H	n-C_3H_7	K	2: 1: 0.08	200 - 205	5	100	86.5
H	$C(CH_3)_3$	K	2.5: 1: 0.1	200 - 210	10	100	86.0
H	$CH(CH_3)_2$ C_2H_5	K	1.9: 1: 0.1	200 *	7	50	43.8
H	$C_{10}H_{17}$	K	1.4: 1: 0.07	200 - 210	9	100	80.4
H	C_6H_5	Na	2: 1: 0.04	110 *	4	0	0
H	C_6H_5	K	2: 1: 0.05	250 *	2	100	90.3
C_2H_5	C_2H_5	K	2: 1: 0.08	200 - 210	10.5	100	84.3
n-C_4H_9	n-C_4H_9	K	1.6: 1: 0.16	200 - 210	11	100	82.2
iso-C_4H_9	iso-C_4H_9	K	2: 1: 0.05	200 - 210	12	100	80.0
C_6H_{11}	C_6H_{11}	K	2: 1: 0.08	210 - 240	13	0	0

EXPERIMENTAL

Triethylsilane has a b.p. of 107.7° (760 mm); d_4^{20} 0.7309; n_D^{20} 1.4121.

The ammonia was evolved from a 30% aqueous solution, dried over solid KOH and collected in a trap, cooled to – 80°. The amines were dried over solid KOH or over metallic sodium, after which they were fractionally distilled.

* The reaction was conducted at ordinary pressure. The temperature indicated is the maximum temperature of the reaction mixture toward the end of the reaction.

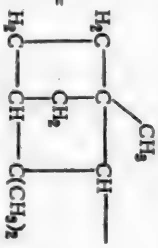
TABLE 2

Physical Properties of the Triethyl(alkylamino)silanes $(C_2H_5)_3SiNHR$ and Triethyl(dialkylamino)silanes $(C_2H_5)_3SiNR_2$. Their Analytical Data and the Molecular Weight Determinations

Formula	Boiling point	Pressure (in mm)	d_4^{20}	n_D^{20}	$n_F^{20}-n_C^{20}$	γ^{20}	M Calc'd	M Found	Silicon content (in %) Calc'd	Silicon content (in %) Found
$(C_2H_5)_3SiNH_2$	137.2°	760	0.7990	1.4279	0.0083	23.10	131.29	128.7	21.38	21.19, 21.22
$(C_2H_5)_3SiNHC_2H_5$*	170.3	760	0.7983	1.4290	0.0085	23.57	159.35	158.1 158.8	17.62	17.38, 17.56
$(C_2H_5)_3SiNHCH_2CH_2CH_3$ ...	189.4	760	0.8038	1.4332	0.0086	24.19	173.37	171.8, 172.0	16.19	15.98, 16.03
$(C_2H_5)_3SiNHCH(CH_3)_2$	179.6	760	0.7962	1.4282	0.0085	22.95	173.37	171.0, 172.4	16.19	15.96, 16.01
$(C_2H_5)_3SiNHC(CH_3)_3$	193.4 - 193.8	760	0.8082	1.4360	0.0081	24.36	187.40	185.2, 185.3	14.99	14.79, 14.87
$(C_2H_5)_3SiNHC(CH_3)_2C_2H_5$ ...	212 - 214	760	0.8194	1.4400	0.0086	25.50	201.42	199.2, 200.4	13.94	13.75, 13.77
$(C_2H_5)_3SiNHC_{10}H_{17}$**	135.0	6	0.9035	1.4775	0.0085	29.14	267.52	264.1, 264.9	10.50	10.28, 10.34
$(C_2H_5)_3SiNHC_6H_5$***	121.0 - 121.5	6	0.9336	1.5210	0.0163	31.89	207.39	205.4, 206.0	13.53	13.33, 13.41
$(C_2H_5)_3SiNHSi(C_2H_5)_3$	243.6 - 244.6	760	0.8461	1.4455	0.0088	25.71	245.56	243.3, 244.0	22.85	22.70, 22.71
$(C_2H_5)_3SiN(C_2H_5)_2$	200.5	760	0.8098	1.4400	0.0087	24.66	187.40	186.5, 187.3	14.99	14.75, 14.80
$(C_2H_5)_3SiN(n\text{-}C_4H_9)_2$	253.2 - 254.2	760	0.8280	1.4475	0.0087	26.33	243.50	242.9, 243.7	11.54	11.33, 11.37
$(C_2H_5)_3SiN(iso\text{-}C_4H_9)_2$	248 - 249.5	760	0.8318	1.4500	0.0084	29.85	243.50	240.6, 241.8	11.54	11.34, 11.39

* Literature data [9]: b.p. 63° (22 mm); d_4^{20} 0.7992; n_D^{20} 1.4290.

** $C_{10}H_{17}$ =



(fenchyl).

*** Literature data [9]: b.p. 130 - 132° (12 mm); d_4^{20} 0.9329; n_D^{20} 1.5210

The methods of the analysis and the determinations of the physical constants were analogous to those described in one of our previous works [5].

Reaction of triethylsilane with ammonia in the absence of catalysts. 11.6 g of triethylsilane and 25 ml of liquid ammonia were heated in an 0.25 liter steel autoclave at 80 - 90° for 6 hours. Hydrogen formation was not observed under these conditions and all the triethylsilane remained unchanged.

Reaction of triethylsilane with ammonia in the presence of sodium amide. a) 0.3 g of metallic sodium and 11.6 g of triethylsilane were added to 40 ml of liquid ammonia. The reaction mixture was stirred at − 35° for 6 hours. After evaporating off the ammonia, 10.5 g of the initial triethylsilane with a b.p. of 108.1° (760 mm) was isolated. b) 30 ml of liquid ammonia, 0.1 g of sodium and 11.6 g of triethylsilane were placed in a 0.25 liter steel autoclave which was cooled to − 65°. The autoclave was heated for 1 hour at 70°. In this period, pressure in the autoclave had risen to 40 atm. After cooling to room temperature, the pressure in the autoclave fell to 20 atm. 2.25 liters of hydrogen were evolved during the reaction and collected in a gasometer. By fractionally distilling the mixture, 6.0 g of triethylaminosilane with a b.p. of 137.5° at 767 mm (yield 45.9 % of the theoretical) and 5.0 g of hexaethyldisilazane with a b.p. of 244 - 245° (767 mm) were isolated. The physical constants of these compounds, which are set forth in Table 2, are in accord with the literature data.

The literature data for triethylaminosilane are [6]: b.p. 137.3°; n_D^{20} 1.4259 [7]. b.p. 134°, n_D^{20} 1.4267.

The literature data for hexaethyldisilazane [2] are: b.p. 100° (1 mm).

Reaction of triethylsilane with ammonia in the presence of potassium amide. 11.6 g of triethylsilane was added to a solution of 1.0 g of potassium in 40 ml of liquid ammonia. The reaction mixture was stirred at − 35° for 8 hours. The excess ammonia was evaporated off and the residue was fractionally distilled; 8.2 g of hexaethyldisilazane with a b.p. of 244.7° (760 mm) were thereby obtained. The yield was 66.8 % of the theoretical.

Reaction of triethylsilane with ammonia in the presence of lithium amide. 30 ml of liquid ammonia, 11.6 g of triethylsilane and 0.3 g of lithium were placed in an 0.25 liter steel autoclave. The autoclave was left at room temperature (20°) for 20 hours. 2.4 liters of hydrogen was evolved as a result of the reaction. 4.5 g (34.3%) of triethylaminosilane with a b.p. of 137.5° at 759 mm and 4.2 g (51.1%) of hexaethyldisilazane with a b.p. of 243.5-244.5° (759 mm) were obtained by fractionally distilling the reaction mixture. Analogous results were obtained by replacing the lithium with 0.5 g of sodium.

Reaction of triethylsilane with sodium amide. 5 g of sodium amide, prepared by dissolving sodium in liquid ammonia [8]* and 11.6 g of triethylsilane were heated to 110° for 11 hours. No reaction was observed under these conditions; hydrogen was not evolved and all the triethylsilane remained unchanged. After redistillation it had a b.p. of 107-108° (758 mm); n_D^{20} 1.4120; d_4^{20} 0.7309.

Synthesis of triethyl(ethylamino)silane. 9.0 g of ethylamine (cooled to −80°), 11.6 g of triethylsilane and 0.1 g of potassium were heated in a 0.25 liter steel autoclave for 2 hours at 80-100°. 2.5 liters of hydrogen was evolved during the reaction and collected in a gasometer. 14.5 g (91.2%) of triethylaminosilane with a b.p. of 170.0° (754.4 mm) was obtained by fractionally distilling the reaction mixture. Its physical constants and analytical data are presented in Table 2.

The following were prepared in an analogous manner by reaction in an autoclave, but at 200-210°: triethyl-(isopropylamino)silane, triethyl(tert-butylamino)silane, triethyl(tert-amylamino)silane, triethyl(fenchylamino)-silane, triethyl(diethylamino)silane, triethyl(di-n-butylamino)silane and triethyl(diisobutylamino)silane. We did not succeed in obtaining all these compounds by the reaction of triethylsilane with the corresponding amines in the presence of the potassium amine derivative at ordinary pressure. The initial triethylsilane did not react in any of these cases.

Reaction of triethylsilane with dicyclohexylamine. 5.8 g of triethylsilane, 18.2 g of dicyclohexylamine and 0.3 g of potassium were heated in an autoclave at 240° for 13 hours. After this period, no further hydrogen evolution occurred. 5.2 g of unchanged triethylsilane and 17.8 g of dicyclohexylamine were isolated by fractionally distilling the reaction mixture.

Synthesis of triethyl(n-propylamino)silane. 0.1 g of finely divided potassium was dissolved by heating in 10.0 g of n-propylamine. 11.6 g of triethylsilane was added to the solution thus obtained. The reaction mixture was heated to boiling for 7 hours in a flask equipped with a reflux condenser, connected, via a Tishchenko bottle containing concentrated sulfuric acid, with a gasometer for collecting the hydrogen. At the end of this period, 2.5 liters of hydrogen had been evolved. By fractionally distilling the reaction mixture, 3.9 g of n-propylamine with a b.p. of 48.0-47.6° (752 mm) and 14.3 g of triethyl-n-propylaminosilane with a b.p. of 189.0° (751.9 mm) were obtained.

Triethyl(phenylamino)silane was obtained in an analogous fashion. Triethylsilane did not react with n-propyl-amine and aniline upon boiling in the presence of metallic sodium.

SUMMARY

The reaction of triethylsilane with ammonia and amines, which is catalyzed by the amides of the alkali metals, was studied. The dependence of the course of the reaction on the nature of the amine and catalyst was shown. The conditions for the synthesis of the amino, alkylamino and dialkylamino derivatives of triethylsilane with high yields were found. 12 compounds of this type were synthesized, 8 of which had been previously unknown, and their physical properties were determined.

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* To completely eliminate the ammonia, the sodium amide obtained was heated in a vacuum at 100° for two hours.

AZO DYES FROM 1,5-AMINONAPHTHOL AND CERTAIN OF ITS DERIVATIVES

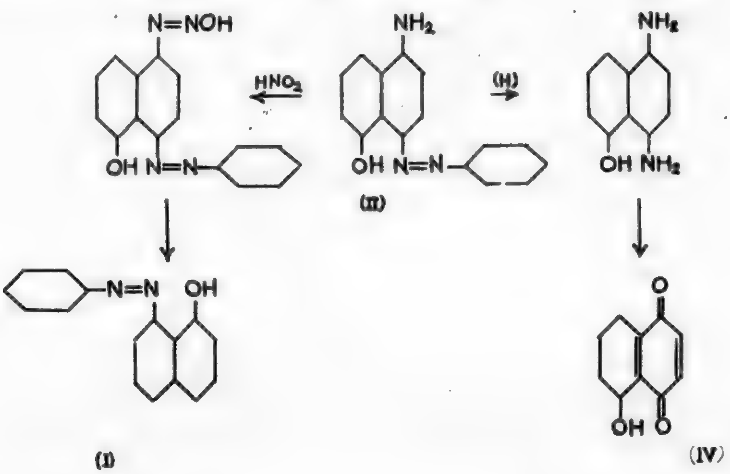
IX. THE HYDROGEN BOND IN CERTAIN PERI-HYDROXY AZO DYES

V. V. Perekalin and Z. S. Segalina

Ortho-hydroxy azo dyes of the naphthalenic series are markedly different in their properties from their isomeric peri-hydroxy azo dyes: in their insolubility or poor solubility in alkaline solutions, in the absence of absorption in the infra-red region which is characteristic of the hydroxy group and in the constant position of the long-wave maxima of the absorption curves during changes of the pH of the medium. The unusual behavior of the ortho-hydroxy azo dyes is to be explained in the light of the representations of tautomerism in the transition of the azoid form of the azo dye into the quinonhydrozone form. At the present time, the specific properties of ortho-hydroxy azo dyes are explained by the existence in them of an intramolecular hydrogen bond [1, 2, 3]. However, in spite of the fact that the hypothesis of hydrogen bonding apparently is in accord with reality, we can nevertheless formally assume tautomerism in the ortho-hydroxy azo dyes and ascribe a quinonhydrozone structure to them.

It is tempting to investigate the properties of those hydroxy azo dyes in which, on structural grounds, one can assume the existence of a hydrogen bond, but in which, on those same grounds, the possibility of azo-hydrozone tautomerism is restricted or entirely excluded. The peri-hydroxy azo dyes of the naphthalenic series are such compounds. In the first place is the simplest para-hydroxy azo dye: 8-benzeneazo-1-naphthol (I), and also 4-benzeneazo-1,5-aminonaphthol (II) and 1-benzeneazo-2,8-aminonaphthol (III).

8-Benzeneazo-1-naphthol (I) was synthesized for the first time from 4-benzeneazo-1,5-aminonaphthol after its diazotization and substitution with hydrogen of the diazo group formed. By combining 1,5-aminonaphthol with diazobenzene in a hydrochloric acid medium, an alkali-insoluble dye was isolated which proved to be not the ortho-hydroxyamino azo dye, but its para-hydroxy isomer—4-benzeneazo-1,5-aminonaphthol (II). Its structure was established by reduction to diaminonaphthol and oxidation of the latter into juglone (IV), which can be formed only if the initial dye was the peri-hydroxy-para-amino azo dye:



(I) (IV)

1-Benzeneazo-2,8-aminonaphthol (III) was prepared according to the preparative directions [4] from 2,8-aminonaphthol and diazobenzene in an acidic medium.

The peri-hydroxy azo dyes investigated by us (I, II and III) had a number of general properties. They were insoluble in alkalis; consequently, their hydroxy groups had considerably less acidic properties than those of the para-hydroxy isomers, which, as is well-known, dissolve readily in dilute alkaline solutions. Change in the pH of the medium did not influence the absorption curves; the position of the long wave maxima of these curves remained constant when the measurements were made in an alcoholic (1) and alcoholic-alkaline medium (2)

(Tables 1, 2 and the figure).*

It must be remembered that the conversion of the neutral molecules of the hydroxy azo dyes, when dissolved in alkalis, into their anions is accompanied by displacement of the position of the long-wave maxima in the visible region [5, 6]. Consequently, the investigated peri-hydroxy azo dyes were not converted by the action of alkali solutions into anions, their hydroxy groups did not react with sodium hydroxide and the hydrogen atoms of the hydroxy groups were without their usual lability.

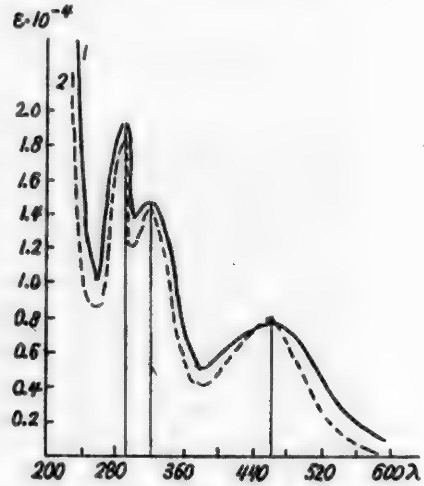


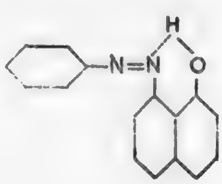
TABLE 1

Dye	λ, mμ	
	ethyl alcohol	ethyl alcohol + NaOH
8-Benzeneazo-1-naphthol	460	460
4-Benzene azo-1,5-aminonaphthol [6]	520	520
1-Benzeneazo-2,8-aminonaphthol [4]	500	500

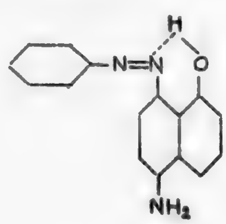
TABLE 2

Dye	Medium	Maxima					
		I		II		III	
		λ	ε	λ	ε	λ	ε
8-Benzene-azo-1-naphthol	ethyl alcohol	290	$1.86 \cdot 10^4$	320	$1.4 \cdot 10^4$	480	$0.775 \cdot 10^4$
	ethyl alcohol + NaOH	290	$1.89 \cdot 10^4$	320	$1.48 \cdot 10^4$	460	$0.76 \cdot 10^4$

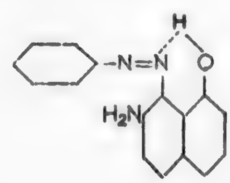
While we can formally use the representation of the slightly probable tautomeric conversion of the azoid form of the dye into the quinonhydrozone form (which does not contain the hydroxy group) to explain this unusually small lability of the hydrogen atoms of the hydroxy groups in the last two peri-hydroxy azo dyes (II and III), a similar conversion is impossible for the simplest para-hydroxy azo dye—8-benzeneazo-1-naphthol (I). Therefore, the lowering of the lability of the hydrogen atoms of the hydroxy groups in the peri-hydroxy azo dyes investigated can be explained by the assumption that the hydrogen atom is supplementarily linked with a nitrogen atom of the azo group, with which it forms a hydrogen bond.



(I)



(II)



(III)

It should be noted that the dyes (I) and (II), in contrast with dye (III), are incapable of forming laks (internal complex salts), which as has been noted previously, may be an indication of the presence of an intramolecular hydrogen bond; however, a negative lak formation reaction would not raise doubts concerning the existence of a hydrogen bond, since not all compounds with hydrogen bonds are capable of forming laks [7].

EXPERIMENTAL

1. Synthesis of 4-benzeneazo-1,5-aminonaphthol (II). 1.59 g of 1,5-aminonaphthol was ground with 1 ml of 37% hydrochloric acid solution and diluted to 200 ml with water (almost all the aminonaphthol went into the solution). 100 ml of an 0.1 N solution of diazobenzene, prepared according to the usual directions, was added over a period of 2 hours to a suspension of 1,5-aminonaphthol, which was being stirred and was at a temperature of 10°. As the diazo compound was added, the solution gradually became red colored and a precipitate of the dye began

* The curves were taken on a SF-11 spectrophotometer by O. M. Dolzhanskaya, to whom we express our gratitude.

to separate from it. After the addition of all the diazo solution, the mixture was stirred for 5 hours more, left overnight and filtered. The dye in the form of a paste which had been washed with water, was triturated with 10 ml of 10% sodium hydroxide solution and diluted to 100 ml with water. The suspension, which had a weakly alkaline reaction, was heated to 50° for 5-10 minutes and filtered after cooling. The alkali-soluble azo dye, 2-benzene-1,5-aminonaphthol was isolated from the alkaline filtrate which had been acidified with dilute acetic acid. The precipitate was washed with water and again treated with alkali. Afaer recrystallization from ethyl alcohol, a finely crystalline brown dye – presumably 4-benzeneazo-1,5-aminonaphthol (II), m.p. 164-165° – was obtained. The dye was insoluble in dilute solutions of sodium hydroxide and dissolved in alcohol with an orange-red color, while in concentrated sulfuric acid it formed a blue solution, which gradually became violet. The yield was 0.42 g (16%).

Reduction of the dye. A saturated weakly alkaline aqueous solution of 1.5 g of hydrosulfite, heated to boiling, was gradually added to a boiling solution of 1 g of the dye in 50 ml of 90% ethyl alcohol; the color of the solution changed from orange-red to light yellow. The diaminonaphthol was not isolated from the solution after filtration, but was oxidized at once.

Oxidation of diaminonaphthol into juglone (IV). A 10% aqueous solution of ferric chloride was gradually added to a solution of 1,4-diamino-5-naphthol at a temperature of 5-7° and the color of the solution became dark red. The juglone which was formed was extracted with chloroform and after evaporating off the solvent, was purified by sublimation; it consisted of a dark brown powder, m.p. 144-147°, dissolved in a 10% solution of sodium hydroxide with a red coloration, which rapidly became brown, and formed a bright red solution in concentrated sulfuric acid.

2. Synthesis of 8-benzeneazo-1-naphthol (I). An equimolecular quantity of sodium nitrite in the form of a saturated solution was gradually added to a blue-violet solution of 1 g of 4-benzeneazo-1,5-aminonaphthol (II) in 50 ml of 95% ethyl alcohol, which was acidified with 2 ml of 96% sulfuric acid and heated to boiling; after the addition of all the sodium nitrite, the color of the solution became light brown. After distilling off some of the alcohol (15-20 ml) and cooling, the mixture was poured out into 100 ml of cold water, and the resinous precipitate was recrystallized from ethyl alcohol. 8-Benzeneazo-1-naphthol consisted of bronze-brown crystals, m.p. 90-92°; quite soluble in ethyl alcohol, insoluble in the cold and on heating with dilute and concentrated solutions of sodium hydroxide; the color of the dyeing with mordanted (with aluminum salts and chrome) and unmordanted wool was identical.

0.0980 g sub.: 0.2790 g CO_2; 0.0418 g H_2O. 0.0988 g sub.: 9.97 ml N_2 (23°, 753 ml). Found %: C 77.4; H 4.84; N 11.3. $C_{16}H_{12}ON_2$. Calculated %: C 77.5; H 4.79; N 11.6.

SUMMARY

1. It was shown that in certain peri-hydroxy azo dyes, in particular, the simplest dye of this series which was synthesized for the first time, 8-benzeneazo-1-naphthol, the hydrogen atom of the hydroxy group lacks its usual lability.

2. A hypothesis was proposed to the effect that in peri-hydroxy azo dyes there is an intramolecular hydrogen bond which explains their specific properties.

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SYNTHESIS OF SULFANILAMIDE DERIVATIVES IN THE LYSINE SERIES

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Lysine (α,ϵ-diaminocaproic acid) is one of the essential amino acids which has great significance for the processes of metabolism and growth in the organism. Its sulfanilyl-substituted derivatives are of undoubted interest for the investigation of their antibacterial action. Due to the two amino groups of lysine, it is possible to obtain the corresponding α- or ϵ-monosulfanilamide, and also the α,ϵ-disulfanilamide derivatives.

In spite of the fact that in diamino acids the aminogroup which is in the alpha position to the carboxyl group has a higher reactivity, the N^{α}-acetyllysine [1, 2] had not been successfully obtained by the direct acetylation of lysine even under mild conditions. Our experiments also confirmed this. We prepared the disulfanilamide derivative in low yield by the condensation of lysine with an equivalent quantity of p-acetylaminobenzensulfo chloride and isolated a very small quantity of N^{α}-(p-acetaminobenzensulfonyl)-lysinefrom the mother liquor. Therefore, in order to prepare the N^{α}- or N^{ϵ}-monosulfanilyl derivative, starting from lysine itself, it was necessary to preliminarily shield the α- or ϵ-amino group.

A method is described in the literature for shielding the ϵ-amino group by the formation of an oxazolidine ring from the carboxyl and α-amino group with the aid of the benzyl ester of chloroformic acid [3].

Racemic N^{α}-(p-aminobenzensulfonyl)-lysine was prepared by Adamson [4]; the ϵ-amino group was shielded by the formation of a homopiperidone ring by heating the methyl ester of lysine at 100°. In view of the low yield (below 10%), the method presents only theoretical interest.

A more convenient method of preparing N^{α}-sulfanylyl-substituted lysine was proposed by Kucherov and Ivanov [5], who prepared optically active N^{α}-(p-aminobenzensulfonyl)-lysines, starting with the corresponding N^{ϵ}-benzoyl derivatives of the lysines which are intermediate products in the isolation of lysine from casein. By the mild alkaline saponification of the N^{ϵ}-benzoyl-N^{α}-(p-acetylaminobenzen sulfonyl)-lysines, the N^{ϵ}-benzoyl bond is ruptured and the corresponding N^{α}-(p-aminobenzen sulfonyl)-lysines are formed. The biological properties of the substances obtained were not indicated.

There is a number of works in the literature involving the use of copper complexes of diamino acids in organic synthesis with the object of shielding the aminogroup [6,7], but this method has not yet been used in syntheses of sulfanylamide derivatives. We succeeded in obtaining N^{α}- and N^{ϵ}-monosulfanilamide derivatives of d,l-lysine with the aid of its copper complex according to the scheme presented on the following page.

The N^{α},N^{ϵ}-bisacetylaminobenzen sulfonyl derivative was obtained by the condensation of lysine with excess p-acetylaminobenzensulfo chloride in an aqueous alkaline medium; its saponification with 15% hydrochloric acid led to N^{α},N^{ϵ}-bis-(p-aminobenzensulfonyl)-lysine. The action of concentrated sulfuric acid on the acetyl derivative in an alcohol medium led simultaneously to saponification and esterification.

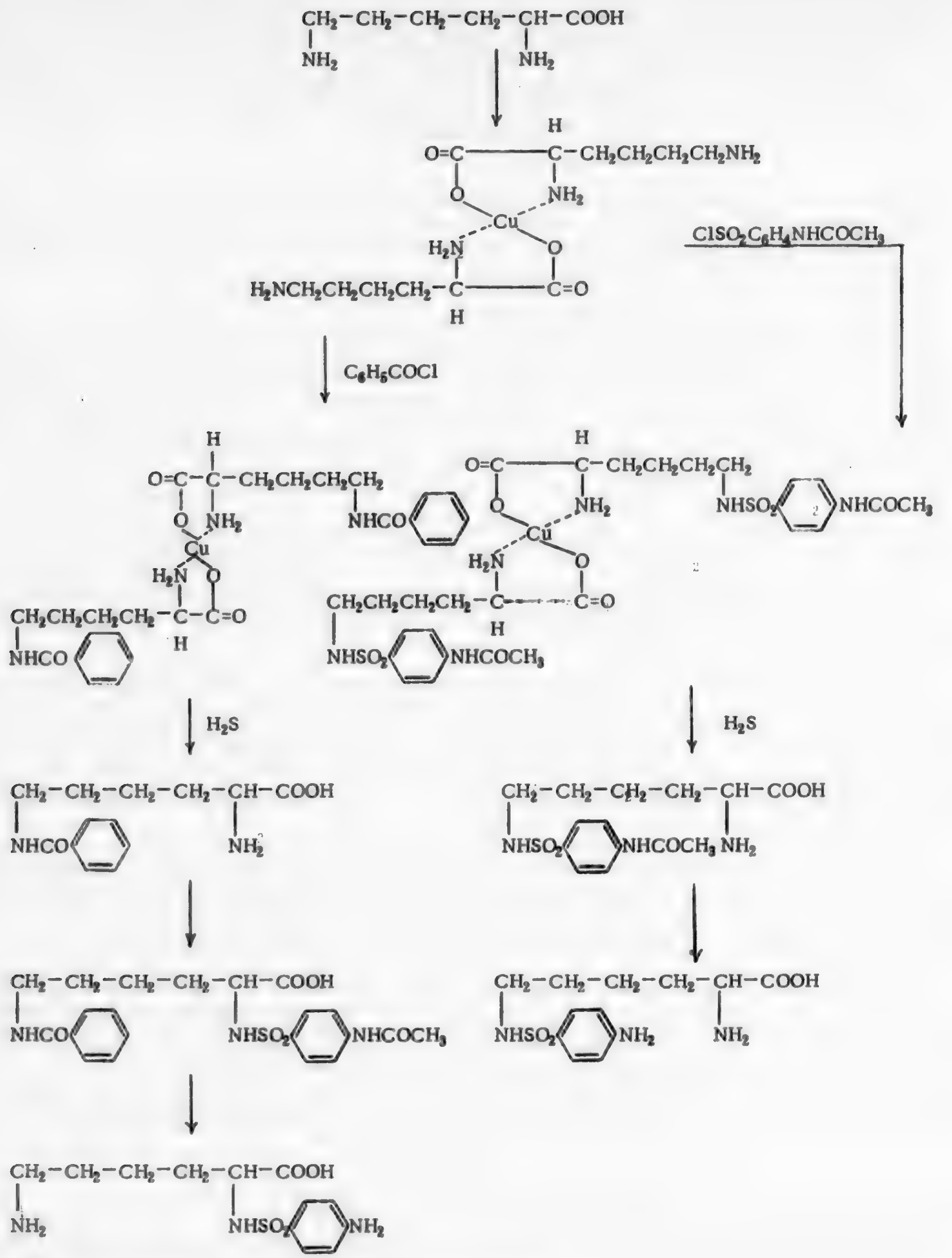
The ethyl ester of d,l-N^{α},N^{ϵ}-bis-(p-aminobenzen sulfonyl)-lysine thus obtained was converted into its hydrazide, from which hydrazones were obtained with p-hydroxybenzaldehyde and with vanillin.

EXPERIMENTAL

N^{α},N^{ϵ}-bis-(p-Acetylaminobenzen sulfonyl)-d,l-lysine

21 g (0.09 mole) of p-acetylaminobenzensulfochloride and 350 ml of 0.5 N sodium hydroxide were simultaneously added over a period of an hour and a half at a temperature not exceeding 35° to a stirred solution of 4.38 g (0.03 mole) of d,l-lysine (m.p. 255-257°) in 150 ml of 0.1 N sodium hydroxide. The mixture was stirred for 5 hours more after the addition of the entire quantity of sulfochloride and alkali. The solution was then filtered off from the unreacted sulfochloride and slowly acidified with concentrated hydrochloric acid (Congo red was the indicator) while it was being energetically stirred. The thick oil which precipitated gradually crystallized on standing for 2 days. The white precipitate obtained was filtered off and washed with 20 ml of water. 13.2 g of a substance with m.p. of 200-202° was obtained. The yield was 81.5% of the theoretical, calculating on the basis of the lysine taken. The substance did not give a blue color with ninhydrin, was quite soluble in 50% alcohol and difficultly soluble in cold water. Upon heating with water, even at 70-80°, the substance was partially decomposed with the evolution of acetic acid. After two-fold recrystallization from a twenty-fold quantity of 50% alcohol, the substance melted at 209-210°.

4.600 mg sub.: 0.432 ml N_2 (27°, 730 mm). 4.287 mg sub.: 3.613 mg $BaSO_4$. Found %: N 10.33; S 11.58. $C_{22}H_{28}O_8N_4S_2$. Calculated %: N 10.37; S 11.85.



N^{α}-N^{ϵ}-bis(p-Aminobenzensulfonyl)-d,l-lysine

A mixture of 12 g of the unpurified acetyl derivative (I) obtained above and 60 ml of 15% hydrochloric acid was heated on a boiling water bath for 1.5 hours. The hot solution was treated with carbon, filtered off and concentrated to dryness in a vacuum at 50-60°. The thick oil obtained was dissolved in 40 ml of water and decolorized with carbon. Sodium acetate was added to the transparent filtrate while it was being stirred until the acid reaction as indicated by Congo red disappeared. The oil which precipitated crystallized after several minutes. 8.5 g of unpurified substance (II) with a m.p. of 181.5-182.5° was obtained. The yield was 85% of the theoretical. After recrystallization from water, the m.p. was 183-184.5°.

7.503 mg sub.: 0.824 ml N_2 (25.5°, 733 mm). 5.933 mg sub.: 6.068 mg $BaSO_4$. Found %: N 12.13; S 14.05. $C_{18}H_{24}O_6N_4S_2$. Calculated %: N 12.28; S 14.04.

Ethyl Ester of N^{α}-N^{ϵ}-bis-(p-Aminobenzensulfonyl)-d,l-lysine

A solution of 4 g of (II) with a m.p. of 181-182° in 40 ml of anhydrous alcohol, saturated with hydrogen chloride, was left for several hours at room temperature. On the following day the reaction mass, in which the white precipitate was formed, was heated on a water bath for 2 hours and then concentrated in a vacuum and 50 ml of water was added to the residue. The solution obtained was decolorized with carbon and neutralized with sodium bicarbonate to disappearance of an acid reaction with Congo red as the indicator, and then a 10% solution of soda was added until the reaction was weakly alkaline to phenolphthalein. The oil which was evolved, crystallized. The precipitate was filtered off and washed with water. The yield was 3.6 g (85%). The ester obtained was very excellently soluble in alcohol, and poorly soluble in water. After two-fold recrystallization from alcohol, the substance had a constant m.p. of 130-131°.

5,704 mg sub.: 10.309 mg CO_2; 2.903 mg H_2O. 6.025 mg sub.: 0.625 ml N_2 (21.5°, 732 mm). Found %: C 49.32; H 5.69; N 11.60. $C_{20}H_{28}O_6N_4S_2$. Calculated %: C 49.59; H 5.78; N 11.57.

A mixture of 2 g of (I)(m.p. 200-202°), 12 ml of alcohol and 1.2 ml of concentrated sulfuric acid was heated on a water bath with a reflux condenser for 4 hours. On cooling to room temperature, a crystalline substance separated from the alcoholic solution. The mixture was poured out into 50 ml of 10% soda solution, which was cooled with ice. The brown oil which separated crystallized after standing for 2 hours. The precipitate obtained was dissolved in 25 ml of 5% hydrochloric acid to separate it from the acid-insoluble acetyl derivative. The acidic solution was treated with carbon and filtered off, after which soda was added until the reaction was alkaline to phenolphthalein. The colorless oil which separated crystallized on standing. The substance was washed with water and recrystallized from 5 ml of alcohol with carbon. The m.p. was 130-131°. The yield was 0.8 g.

Hydrazide of N^{α}-N^{ϵ}-bis-(p-Aminobenzensulfonyl)-d,l-lysine

1 ml of 85% hydrazine hydrate was added to a hot solution of 1.55 g of the ethyl ester (II) in 30 ml of 95% alcohol. The solution was boiled on a water bath and then the alcohol solution together with the small precipitate which formed was concentrated to dryness in a vacuum. The substance obtained was washed with 10 ml of alcohol to eliminate the excess hydrazine hydrate. 1.35 g of a substance with a m.p. of 209-212° was obtained. The hydrazide was poorly soluble in alcohol and in water. After recrystallization from 50% alcohol the m.p. was 217-218°.

3.245 mg sub.: 5.499 mg CO_2; 1.610 mg H_2O. 3.600 mg sub.: 0.555 ml N_2 (20°, 734 mm). Found %: C 46.25; H 5.55; N 17.34. $C_{18}H_{26}O_5N_6S_2$. Calculated %: C 46.00; H 5.53; N 17.87.

o-Hydroxybenzalhydrazide of N^{α}-N^{ϵ}-bis-(p-Aminobenzensulfonyl)d,l-lysine

1.3 ml of salicylic aldehyde was added to a solution of 0.5 g of the hydrazide (IV) (m.p. 217-218°) in 55 ml of hot 50% alcohol, and the mixture was heated for an hour and a half. On the following day the yellow precipitate which was formed was filtered off and washed with water, alcohol and ether. After recrystallization from 50% alcohol, in which it was very slightly soluble, the hydrazone had a m.p. of 156°.

3.026 mg sub.: 5.830 mg CO_2; 1.300 mg H_2O. Found %: C 52.58; H 4.80. $C_{25}H_{30}O_6N_6S_2$. Calculated %: C 52.26; H 5.23.

p-Hydroxy-m-methoxybenzalhydrazide of N^{α}-N^{ϵ}-bis-(p-Aminobenzensulfonyl)-d,l-lysine

A solution of 0.3 g of vanillin in 12 ml of alcohol was added to a hot solution of 1.2 g of the hydrazide (IV) in 140 ml of 50% alcohol. The mixture was heated on a water bath for an hour and a half. The solution was concentrated in a vacuum until a white precipitate appeared, which was filtered off and recrystallized from 50% alcohol. The m.p. was 143-146° and the weight 1.5 g.

N^{ϵ}-Benzoyl-d,l-lysine

12 g of copper carbonate was gradually added over a period of 15 minutes to a solution of 6 g of d,l-lysine in 180 ml of water, which was heated to 80° and stirred. The mixture was stirred for 15 minutes more and then the hot blue solution was filtered off from the unreacted copper salt; the precipitate was washed with small portions of water. After cooling, initially 3 ml of 40% sodium hydroxide and then, gradually, from a separatory funnel, 6 ml of freshly distilled benzoyl chloride over a period of 15 minutes, were added to the transparent filtrate after cooling, and while it was being energetically stirred. The alkalinity of the reaction mass was maintained by the addition of 6 ml of 40% sodium hydroxide (in 0.5 mm portions). A blue precipitate fell out, but the aqueous layer was still bluish in color. 1.5 ml more of benzoyl chloride and 2.5 ml of 40% sodium hydroxide were added, after which the aqueous layer became almost colorless. The stirring was continued for 12 hours. The blue precipitate of the

copper complex of N^{ϵ}-benzoyl-d,l-lysine (14.8 g of the crude product) was filtered off and washed with a 5% solution of soda to eliminate the benzoic acid formed. The suspension of the copper complex obtained in 200 ml of 2% hydrochloric acid was saturated with hydrogen sulfide. The precipitate of cuprous sulfide formed was filtered off, the colorless filtrate was neutralized with a 40% solution of sodium hydroxide until the solution was no longer acid to Congo red (in the absence of a reaction which was alkaline to phenolphthalein); a white precipitate thereupon fell out which, after washing with water and recrystallization from 50% alcohol, had a decomposition temperature of 252-254°, which is in accord with the literature data for N^{ϵ}-benzoyl-d,l-lysine [8, 9]. The substance obtained gave a blue color with ninhydrin, which indicates the presence of the free α-amino group. The yield was 3.2 g (31.2%), calculating on the basis of the lysine taken.

N^{α}-(p-Acetylaminobenzensulfonyl)-N^{ϵ}-benzoyl-d,l-lysine

A mixture of 3.2 g of the benzoyl derivative (VII) and 65 ml of 0.1 N sodium hydroxide solution was stirred for 2 hours. A white paste thereupon formed, to which was added 5.9 g of p-acetylaminobenzensulfochloride and 105 ml of 0.5 N sodium hydroxide in order to keep the reaction mass alkaline to phenolphthalein. After 6 hours, almost all the sulfochloride dissolved. The unreacted sulfochloride was filtered off, and the filtrate was slowly rendered acidic to Congo red with hydrochloric acid while it was being energetically stirred. The oil which thereupon separated out, crystallized. The residue was filtered off, washed with cold water and dried. The substance obtained had a m.p. of 226-228°. The yield was 4.2 g (73.5%), calculating on the basis of the initial benzoyl derivative. The substance did not give a color with ninhydrin. The substance was recrystallized from 50% alcohol for analysis. It consisted of fine flakes, m.p. 227-229°.

7.056 mg sub.: 4.67 ml 0.1 N H_2SO_4 (Kjeldahl). Found %: N 9.26. $C_{21}H_{25}O_6N_3S$. Calculated %: N 9.39.

N^{α}-(p-Aminobenzensulfonyl)-d,l-lysine

A solution of 3.2 g of the acetyl derivative (VIII) (m.p. 226-228°) in 100 ml of 1 N sodium hydroxide was heated on a boiling water bath for 15 hours. After cooling, the solution was filtered off and the filtrate was acidified with concentrated hydrochloric acid (Congo red). The acidic solution was concentrated to dryness in a vacuum and the residue thrice extracted with 0.5 N hydrochloric acid in 33 ml portions. The combined extract was carefully neutralized with a concentrated solution of ammonia with litmus as the indicator. After two days, a precipitate fell out which did not melt at 300°. The yield was 1.2 g (56%), calculating on the basis of the acetyl derivative. The substance obtained, after recrystallization from 50 ml of water, decomposed at 280-282°, (according to Adamson [4], 286°).

3.342 mg sub.: 5.839 mg CO_2; 1.930 mg H_2O. 4.750 mg sub.: 0.598 ml N_2 (21°, 727 mm). Found %: C 47.67; H 6.46; N 13.99. $C_{12}H_{19}O_4N_3S$. Calculated %: C 48.00; H 6.33; N 14.00.

N^{ϵ}-(p-Acetylaminobenzensulfonyl)-d,l-lysine

A solution of 12 g of d,l-lysine in 320 ml of water was heated to 80° while being stirred, and 24 g of copper carbonate was added to it over a period of 20 minutes, after which the mixture was stirred for 40 minutes more at 75-80°. The hot blue solution was filtered off, and to the blue filtrate after cooling was added initially 20 ml of 2 N sodium hydroxide and then 21 g of p-acetylaminobenzensulfochloride (10% excess) over a period of 20 minutes and while the solution was being stirred. The mixture was then stirred at room temperature for 15 hours; 30 ml more of 2 N sodium hydroxide was thereupon added in order to keep the reaction mixture consistently alkaline to phenolphthalein. After filtration, the blue precipitate (62 g of the crude product) was dissolved in 1 liter of 2% hydrochloric acid. Hydrogen sulfide was passed into the acidic solution of the copper complex obtained until the formation of cuprous sulfide ceased. Then the mixture was heated on a water bath at 70-80° for an hour and a half. After filtration from the cuprous sulfide, the solution was decolorized with carbon and concentrated to dryness in a vacuum. The substance obtained was twice recrystallized from 50% alcohol, for analysis. M.p. was 251-252°.

7.425 mg sub.: 0.817 ml N_2 (22°, 725 mm). Found %: N 12.14. $C_{14}H_{21}O_4N_3S$. Calculated %: N 12.24.

N^{ϵ}-(p-Aminobenzensulfonyl)-d,l-lysine

The acetyl derivative obtained (X) was heated with 100 ml of 15% hydrochloric acid at 85-90° for 1.5 hours. The solution was then concentrated to dryness in a vacuum. The residue was dissolved in 150 ml of water and neutralized with a saturated solution of soda. The substance isolated (11.7 g) was recrystallized from 80 ml of 50% alcohol and 9.2 g (37.5%) calculating on the lysine) was obtained. The substance was once more recrystallized from a ten-fold quantity of 50% alcohol for analysis. The m.p. was 204-205° (with decomposition).

6.462 mg sub.: 0.804 ml N_2 (25.5°, 738 mm). Found %: N 13.83. $C_{12}H_{19}O_4N_3S$. Calculated %: N 14.00.

SUMMARY

1. The N^{α}- and N^{ϵ}-sulfanilyl-substituted d,l-lysines were synthesized via their copper complex.

2. N^{α},N^{ϵ}-disulfanilyl-substituted d,l-lysine and the corresponding ester, hydrazide and hydrazones were prepared.

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ALKAMINE ESTERS OF β-(4-HYDROXYPHENYL)-α-PHENYLPROPIONIC ACID

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The valuable spasmolytic properties of the alkamine esters of diphenylacetic acid led to the introduction into practical medicine of the preparation "Trasentine" (spasmolytin) [1] and "Tropacine" [2]. The introduction into the aliphatic chain of a hydroxyl group and the conversion, thereby, into a series of benzilic acids, preserves the capacity of the diphenylmethane grouping to be the carrier of the valuable biological properties. Thus, the alkamine esters of benzilic acid [3] differ little in their spasmolytic action from the corresponding esters of diphenylacetic acid. We were interested in the question of the extent to which the bond of the two phenyl radicals with a single carbon atom was necessary for the alkamine ester to possess neurotropic activity.

The benzhydrylamine $(C_6H_5)_2CHNH_2$ is a highly active pharmacological substance and has anesthetic activity [4,a]. Its 3,3'-dipropylhydroxy derivative is 20 times more powerful as an anesthetic than novocain [4, 6]. 1,2-Diphenylethylamine $C_6H_5CH_2(C_6H_5)CHNH_2$ also possesses anesthetic activity and is a pharmacologically active substance [5]. One can conclude from a comparison of these compounds that α,β-diphenylpropionic acid also may serve as a carrier of neurotropic activity, while its alkamine esters can have a spasmolytic effect. If we consider the spasmolytic preparation as a heteropole in which there is, on the one hand, a basic group, for example, an aliphatic amine, and on the other hand, a group with an acidic character, then almost all spasmolytics fit in this scheme. A certain strengthening of the action of the phenyl group in such a heteropole via the introduction of a hydroxyl group into it may have been favorable for the spasmolytic effect. On the basis of these considerations, the alkamine esters of β-(4-hydroxyphenyl)-α-phenylpropionic acid, in which the heteropolar action of the phenyl groups is stretched out over the entire length of the propionic chain, served as the subject of the investigation.

β-(4-Hydroxyphenyl)-α-phenylpropionic acid was obtained for the first time [6] by the reduction with sodium of 4-hydroxy-α-phenylcinnamic acid, which, in turn, was prepared by boiling 4-hydroxybenzaldehyde with sodium phenylacetate in an acetic anhydride medium [7].

Since anisaldehyde is more accessible than 4-hydroxybenzaldehyde, it was more convenient for us to prepare β-(4-hydroxyphenyl)-α-phenylpropionic acid via the acrylic acid [8, 9]:

$$p\text{-}C_6H_4\begin{matrix}\nearrow CHO\\ \searrow OCH_3\end{matrix} + C_6H_5CH_2COONa + (CH_3CO)_2O \longrightarrow (p\text{-}C_6H_4OCH_3)CH{=}C\begin{matrix}\nearrow C_6H_5\\ \searrow COOH\end{matrix}$$

with subsequent hydrogenation and demethylation.

The condensation of anisaldehyde with sodium phenylacetate to form the corresponding acrylic acid is conducted with the aid of a 5-fold quantity of acetic anhydride at 170-180° [9]. It proved possible to make these conditions more mild: the acetic anhydride can be taken in an equimolecular quantity, calculating on the basis of the anisaldehyde; the temperature can be lowered to 100°, although this requires a certain lengthening of the condensation process.

For the conversion to the substituted propionic acid, the authors hydrogenated the sodium salt of β-(4-methoxyphenyl)-α-phenylacrylic acid in the presence of a porous nickel catalyst in an aqueous-alcoholic medium at 3 atm for 28 hours. The β-(4-methoxyphenyl)-α-phenylpropionic acid obtained by them had a m.p. of 105-107°. The yield was 93% of the theoretical. Faltis and others [10] carried out the hydrogenation with a palladium catalyst for 4 hours, and obtained acid with a m.p. of 120-121° after recrystallization from alcohol.

To demethylate the β-(4-methoxyphenyl)-α-phenylpropionic acid obtained, they heated it with a mixture of 48% hydrobromic acid and glacial acetic acid for 6.5 hours and obtained the hydroxy acid with a m.p. of 177-178° [9] in a yield of 88%. Bakunin [6] demethylated the acid with the aid of hydriodic acid and obtained a hydroxy acid with a m.p. of 177°.

We combined both processes in our work – that of hydrogenation and that of demethylation – replacing the acidic demethylation with an alkaline demethylation. The hydrogenation was carried out by us in an aqueous

medium at 100°, while the demethylation was carried out at 220-225° with the aid of potassium hydroxide. The β-(4-hydroxyphenyl)-α-phenylpropionic acid which was obtained had a m.p. of 177°. The yield based on the initial methoxycinnamic acid was 94% of the theoretical.

We prepared the alkamine esters by two methods:

a) reaction of the acid chloride of the acid with the alkamine alcohol;

b) transesterification of the ethyl ester of β-(4-hydroxyphenyl)-α-phenylpropionic acid into the alkamine ester in the presence of a small quantity of metallic sodium.

The method of transesterification gives low yields of the esters, but in the method with the acid chloride we encountered the difficulty that during the action of thionyl chloride on β-(4-hydroxyphenyl)-α-phenylpropionic acid, a substance is formed which we could not isolate in the pure form; consequently, after the elimination of excess thionyl chloride from the reaction mass, the entire residue was introduced in the reaction with the alkamine alcohol.

The preparation proceeds considerably better if the phenol group is shielded with an acetyl radical. Then the pure acid chloride of β-(4-acetoxyphenyl)-α-phenylpropionic acid, with which the reaction of formation of the alkamine ester proceeds normally, can be isolated.

EXPERIMENTAL

β-(4-Methoxyphenyl)-α-phenylacrylic Acid

196 g of sodium phenylacetate (1.24 moles), 150 g of acetic anhydride (1.47 moles) and 195 g of commercial anisaldehyde which contained 81.5% of the pure aldehyde, were placed in a three-necked flask with a stirrer. The mixture was heated while being stirred for 45 hours at 100°. Upon cooling to 80°, 20 ml of water was carefully added, the mixture was left for 0.5 hour, and then 250 ml more of water was again carefully added. After stirring well and cooling, theprecipitate which settled out was filtered off, washed with water and pressed out well. The precipitate was transferred to a dish, blended with 200 ml of methyl alcohol, filtered off again and once more washed with 200 ml of methyl alcohol. The acid filtered off was dissolved in 250 ml of 5% sodium carbonate solution, heated to boiling for 30 minutes with 10 g of carbon, filtered off from the carbon, and the filtrate was poured during stirring into 250 ml of 20% hydrochloric acid. The acid which precipitated after cooling was filtered off, washed with water and dried at 100°. 200 g (67.3%) of β-(4-methoxyphenyl)-α-phenylacrylic acid, calculating on the gasis of the anisaldehyde, was obtained and had a m.p. of 186-188°.*

β-(4-Hydroxyphenyl)-α-phenylpropionic Acid

300 g of β-(4-methoxyphenyl)-α-phenylacrylic acid, 1500 ml of water, 60 g of sodium hydroxide and 30 g of nickel catalyst were placed in a rotating 3-liter autoclave. The autoclave was then filled with hydrogen to a pressure of 60 atm. The material was hydrogenated for 4 hours at 90-100°. Upon cooling the autoclave, the catalyst was filtered off, and the filtrate was again placed in the autoclave, to which 420 g of sodium hydroxide was added. The autoclave was heated at 220° for 15-16 hours. The solution of the salt of β-(4-hydroxyphenyl)-α-phenylpropionic acid obtained was filtered and the filtrate was treated with hydrochloric acid until the reaction was acid. 270 g (94.4%) of a substance in the form of a fine white powder with a m.p. of 176-177° was obtained.**

Ethyl β-(4-Hydroxyphenyl)-α-phenylpropionate

A mixture of 6 g of β-(4-hydroxyphenyl)-α-phenylpropionic acid, 12 ml of anhydrous ethyl alcohol and 3 ml of concentrated sulfuric acid was heated on a water bath for 5 hours at the boiling point. Upon completion of the reaction, the mass was poured out into water. The precipitate which settled out was filtered off, washed with water, and then with 5% soda solution and again with water. After recrystallization from alcohol, 6.5 g (96%) with a m.p. of 77-78° was obtained. It consisted of white crystals, soluble in alcohol, ether, benzene and insoluble in water and soda.

3.06 mg sub.: 8.483 mg CO_2; 1.866 mg H_2O. Found %: C 75.48; H 6.81. $C_{17}H_{18}O_3$. Calculated %: C 75.55; H 6.66.

β-(4-Acetoxyphenyl)-α-phenylpropionic Acid

A mixture of 40 g of β-(4-hydroxyphenyl)-α-phenylpropionic acid, 50 g of acetic anhydride and 0.5 ml of concentrated sulfuric acid was heated at the boiling point with a reflux condenser for 7 hours. The reaction

* Ogliloro [8] indicates a m.p. of 188-189°; Baker and Sansbury [9], a m.p. of 186°.

** Bakunin [6] indicates a m.p. of 179-180°; Baker and Sansbury [9], a m.p. of 172-175°.

mass was then poured out into water. The oil which separated crystallized on standing. After recrystallization from 80% acetic acid, 35 g (74.5%) with a m.p. of 143-145° was obtained. The substance was soluble in alkali, acetone and hot acetic acid and was insoluble in water.

4.323 mg sub.: 11.340 mg CO_2; 2.094 mg H_2O. Found %: C 71.77; H 5.42. $C_{17}H_{16}O_4$. Calculated %: C 71.80; H 5.63.

Acid Chloride of β-(4-Acetoxyphenyl)-α-phenylpropionic Acid

A mixture of 10 g of β-(4-acetoxyphenyl)-α-phenylpropionic acid and 8.2 g of thionyl chloride was heated at 55-60° while being stirred, for 3 hours. After cooling, the reaction mass crystallized. The crystals were recrystallized from benzene.

The substance consisted of white needles with a m.p. of 91-93° (with decomposition). The yield was 9.5 g (90%).

The substance was soluble in benzene and ether and difficultly soluble in petroleum ether.

6.733 mg sub.: 2.300 mg AgCl. Found %: Cl 11.55. $C_{17}H_{15}O_3Cl$. Calculated %: Cl 11.73.

Acid Chloride of β-(4-Hydroxyphenyl)-α-phenylpropionic Acid

A solution of 10 g of β-(4-hydroxyphenyl)-α-phenylpropionic acid and 89.5 ml of 0.454 N alcoholic potassium hydroxide was concentrated to dryness in a vacuum. 10 g of thionylchloride was added to the dry residue. The mixture was heated for 1 hour at 50°; under these conditions the mass strongly effervesced. The excess thionyl chloride was then driven off in a vacuum. The residue, which was in the form of a hard brittle mass, could not be purified as a consequence of decomposition. It was converted into the amide.

Amide of β-(4-Hydroxyphenyl)-α-phenylpropionic Acid

The residue obtained above was stirred with 25 ml of 23% ammonia in methyl alcohol. The mixture was left for 48 hours. The crystals which formed were recrystallized from hot water.

The substance consisted of white crystals with a m.p. of 180-182°. The crystals were soluble in hot water and insoluble in cold water and alcohol.

6.588 mg sub.: 0.325 ml N_2 (19°, 728 mm). Found %: N 5.53. $C_{15}H_{15}O_2N$. Calculated %: N 5.80.

2-N,N-Dimethylaminoethyl β-(4-Hydroxyphenyl)-α-phenylpropionate

A solution of 0.4 g of metallic sodium in 20 g of dimethylaminoethanol was added to a solution of 5 g of ethyl β-(4-hydroxyphenyl)-α-phenylpropionate in 10 g of dimethylaminoethanol. The mixture was heated for 30 minutes, at 140°. 23 g of excess dimethylaminoethanol was then driven off in a vacuum. The residue was treated with dilute hydrochloric acid until the reaction was acid to Congo red and was extracted with ether. The ethereal extract was washed with a soda solution from which 2.4 g of β-(4-hydroxyphenyl)-α-phenylpropionic acid was isolated by acidification with hydrochloric acid.

0.5 g of ethyl β-(4-hydroxyphenyl)-α-phenylpropionate was obtained from the ethereal extract by driving off the ether.

The aqueous hydrochloric acid solution was neutralized with soda and then extracted with ether. After drying and driving off the ether, 1.5 g of dimethylaminoethyl β-(4-hydroxyphenyl)-α-phenylpropionate was obtained. The substance was recrystallized from alcohol: m.p. 115-116°. It was soluble in alcohol, hydrochloric acid and alkali and insoluble in soda solution and water.

7.585 mg sub.: 0.305 ml N_2 (25.5°, 729 mm). 5.335 mg sub.: 0.211 ml N_2 (25.5°, 729 mm). Found %: N 4.40, 4.34. $C_{19}H_{23}O_3N$. Calculated %: N 4.46.

Hydrochloride. The theoretical quantity of hydrogen chloride in anhydrous alcohol was added to the solution of base obtained. A white crystalline precipitate settled out with a m.p. of 150-152° (decomposition). It was quite soluble in water and insoluble in anhydrous alcohol and ether.

Found %: N 4.08. $C_{19}H_{23}O_3N \cdot HCl$. Calculated %: N 4.06.

Hydrobromide. The m.p. was 164-166° (with decomposition). It was soluble in water and insoluble in anhydrous alcohol and ether.

8.165 mg sub.: 0.273 ml N_2 (24.5°, 730 mm). 2.646 mg sub.: 1.283 mg AgBr. Found %: N 3.68; Br 20.60. $C_{19}H_{23}O_3N \cdot HBr$. Calculated %: N 3.57; Br 20.29.

2-N,N-Diethylaminoethyl β-(4-Hydroxyphenyl)-α-phenylpropionate

A solution of 10 g of β-(4-hydroxyphenyl)-α-phenylpropionic acid in 89.5 ml of 0.454 N alcoholic potassium hydroxide was concentrated to dryness in a vacuum. 10 g of thionyl chloride in 10 ml of dry benzene was added to the dry residue. The mixture was heated at 50° for 1 hour; under these conditions the mass strongly foamed. The excess of thionyl chloride was then driven off in a vacuum. Benzene and 20 ml of diethylaminoethanol were then added to the residue, which had the form of a hard, brittle mass. The reaction mixture was stirred and heated for 4 hours at the boiling point. The benzene and diethylaminoethanol were then driven off in a vacuum. The residue was diluted with water, neutralized with soda solution and extracted with ether. 2 g of the initial acid was recovered from the soda solution. The hydrochloride, which solidified with difficulty, was isolated from the ethereal extract after drying over anhydrous sodium sulfate and adding an alcoholic solution of hydrogen chloride; it was recrystallized from acetone. The yield was 4 g; m.p. 127-129° (with decomposition). It was quite soluble in water and hot acetone and was insoluble in anhydrous alcohol and ether.

9.395 mg sub.: 0.277 ml N_2 (28.5°, 720 mm). 3.378 mg sub.: 1.305 mg AgCl. Found %: N 3.58; Cl 9.56. $C_{21}H_{27}O_3N \cdot HCl$. Calculated %: N 3.71; Cl 9.40.

Hydrobromide. The m.p. was 139-141° (decomposition). It was soluble in water and hot acetone and insoluble in anhydrous ether and alcohol.

8.420 mg sub.: 0.258 ml N_2 (27.5°, 727 mm). 3.796 mg sub.: 1.697 mg AgBr. Found %: N 3.32; Br 19.02. $C_{21}H_{27}O_3N \cdot HBr$. Calculated %: N 3.31; Br 19.94.

The isolated base had a m.p. of 65-66°. It was insoluble in water and soluble in ether, alcohol and other organic solvents.

5.335 mg sub.: 0.211 ml N_2 (25.5°, 729 mm): Found %: N 4.34. $C_{21}H_{27}O_3N$. Calculated %: N 4.10.

3-N,N-Dimethylaminopropyl β-(4-Hydroxyphenyl)-α-phenylpropionate

It was prepared from 5 g of ethyl β-(4-hydroxyphenyl)-α-phenylpropionate and 10 g of dimethylaminopropanol analogously to the dimethylaminoethyl ester. After drying and distilling off the ester, 0.7 g of the base, which could not be crystallized and purified, was obtained. It was dissolved in ethyl acetate and neutralized with a solution of hydrogen chloride in anhydrous ether. The hydrochloride which precipitated was recrystallized from ethyl acetate. The m.p. was 140-141° (with decomposition).

7.100 mg sub.: 0.245 ml N_2 (22°, 734 mm). 8.335 mg sub.: 0.287 ml N_2 (22°, 734 mm). Found %: N 3.91, 3.85; $C_{20}H_{25}O_3N \cdot HCl$. Calculated %: N 3.87.

3-N,N-Diethylaminopropyl β-(4-Hydroxyphenyl)-α-phenylpropionate

It was prepared from 5 g of the ethyl β-(4-hydroxyphenyl)-α-phenylpropionate and 12 g of 3-diethylaminopropanol analogously to the preceding. The base isolated from the alkamine ester did not crystallize. It was dissolved in ethyl acetate and neutralized with a solution of hydrogen bromide and anhydrous alcohol. The hydrobromide crystallized out on prolonged standing. After recrystallization from ethyl acetate, the m.p. was 134° (with decomposition). It consisted of a crystalline substance, quite soluble in water and hot ethyl acetate and insoluble in anhydrous alcohol and ether.

8.885 mg sub.: 0.265 ml N_2 (24°, 732 mm). 6.480 mg sub.: 0.190 ml N_2 (24°, 732 mm). 4.912 mg sub.: 2.134 mg AgBr. Found %: N 3.30, 3.25; Br 18.49. $C_{22}H_{29}O_3N \cdot HBr$. Calculated %: N 3.21; Br 18.33.

2-N,N-Diethylaminoethyl β-(4-Acetoxyphenyl)-α-phenylpropionate

4 g of diethylaminoethanol was added to a stirred solution of 9.7 g of the acid chloride of β-(4-acetoxyphenyl)-α-phenylpropionic acid in 25 ml of dry toluene. The mixture was heated for 4 hours at the boiling point of toluene. After cooling, dilute hydrochloric acid was added to the reaction mass.

2 g of the initial acid was isolated from the toluene layer after drying and distillation. The acidic layer was neutralized with a 5% solution of alkali and extracted with ether. After drying and driving off the ether, 8.5 g of the base was isolated in the form of a thick oil. It was dissolved in ethyl acetate and treated with an alcoholic solution of hydrogen bromide. The hydrobromide which was isolated after recrystallization from ethyl acetate had a m.p. of 134-135° (decomposition). It consisted of a white crystalline substance, which was quite soluble in water and hot ethylate; it was insoluble in ether.

9.355 mg sub.: 0.260 ml N_2 (24°, 736 mm). 8.413 mg sub.: 0.237 ml N_2 (25°, 733 mm). Found %: N 3.09, 311. $C_{23}H_{29}O_4N \cdot HBr$. Calculated %: N 3.08.

The hydrochloride, recrystallized from ethyl acetate, had a m.p. of 127° (with decomposition).

7.915 mg sub.: 0.261 ml N_2 (30°, 733 mm). 8.150 mg sub.: 0.262 ml N_2 (30°, 735 mm). 14.318 mg sub.: 1.77 ml $AgNO_3$. 14.318 mg sub.: 1.77 ml $AgNO_3$. Found %: N 3.57, 3.49; Cl 8.96, 8.77. $C_{23}H_{29}O_4N \cdot HCl$. Calculated %: N 3.33; Cl 8.46.

SUMMARY

The dimethylaminoethyl, diethylaminoethyl, dimethylaminopropyl and diethylaminopropyl esters of β-(4-hydroxyphenyl)-α-phenylpropionic acid, and also the diethylaminoethyl ester of β-(4-acetoxyphenyl)-α-phenylpropionic acid and other compounds were synthesized.

The specified esters may have valuable biological properties.

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SYNTHESIS OF p-NITRO-o-ANISIDINE VIA DIARYLUREA AND ITS DINITRO DERIVATIVE

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p-Nitro-o-anisidine (2-methoxy-4-nitroaniline) or, as it is called in technology, azoamine rose O, appears in the aniline dye industry as an intermediate product in the preparation of synthetic insoluble azo dyes on the fiber. A method worked out by Soviet authors [1] for nitrating the N-arylsulfonyl derivative of o-anisidine with 10% dilute nitric acid with heating to 80° lies at the base of its industrial preparation.

The starting material for the preparation of p-nitro-o-anisidine is o-anisidine, which undergoes alkylation and nitration with subsequent hydrolysis of the nitro-derivative.

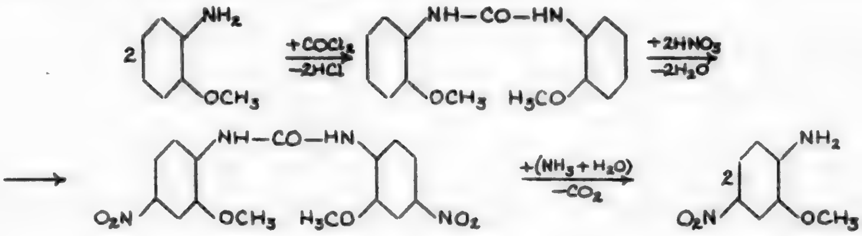
p-Toluenesulfochloride is used as the acylating agent.

The use of p-toluenesulfochloride as the acylating agent makes the production considerably more expensive in comparison with processes in which, for example, acetic or formic acid is used as the acylating agent.

In addition, the last phase of the process – the hydrolysis of arylsulfonnitroanilide with 80% sulfuric acid at 135-150° or with concentrated sulfuric acid in the cold – presents certain difficulties, since it is accompanied by side reactions: sulfonation, the formation of sulfones and resinification.

In view of this, we worked out a new method for preparing p-nitro-o-anisidine via diarylurea and its dinitro derivative. The cheap and quite accessible phosgene is used as the acylating agent in this case.

The acylation of o-anisidine with phosgene proceeds readily with the formation of 2,2'-dimethoxydiphenylurea; upon nitration of the latter with nitric acid, 4,4'-dinitro-2,2'-dimethoxydiphenylurea is formed; p-nitro-o-anisidine is obtained by its hydrolysis under appropriate conditions:



We phosgenated o-anisidine in an aqueous medium at 40°; the yield of 2,2'-dimethoxydiphenylurea amounted to 98.5-98.8% of the theoretical.

2,2'-Dimethoxydiphenylurea was nitrated with weak nitric acid in an aqueous suspension at high temperature, which resulted in the formation chiefly of 4,4'-dinitro-2,2'-dimethoxydiphenylurea and only in very insignificant quantity of the isomeric 6,6'-dinitro-2,2'-dimethoxydiphenylurea. 5,5'-Dinitro-2,2'-dimethoxydiphenylurea was not formed at all [2].

4,4'-Dinitro-2,2'-dimethoxydiphenylurea was obtained in a yield of 92.1-93.2% of the theoretical as a result of the nitration of 2,2'-dimethoxydiphenylurea by this method.

The last stage of the process is the hydrolysis of 4,4'-dinitro-2,2'-dimethoxydiphenylurea.

There are indications in the literature [3] to the effect that the hydrolysis of diphenylurea and its substituted derivatives proceeds better in an alcoholic ammonia solution heated under pressure. Gershzon and Lastovsky [4] found that di-o-tolylurea, which is slightly changed by treatment with acid or alkali at ordinary pressure, is almost completely hydrolytically decomposed in an acidic medium under increased pressure.

In preceding works [5] we have studied in detail the hydrolysis of diphenylurea and its dinitro-derivative, both in acidic and in alkaline media and have shown that an aqueous ammonia solution is a better hydrolyzing agent. The indicated ureas are almost completely hydrolyzed in a dilute ammonia solution at 150° under increased pressure, and the reaction products obtained as a result have a melting point which is very close to that indicated in the literature. These data are completely confirmed in the present work.

Our experiments showed that the hydrolysis of 4,4'-dinitro-2,2'-dimethoxydiphenylurea in a medium of 1% aqueous ammonia at 150° and under increased pressure, proceeds very readily and yields 2-methoxy-4-nitroaniline in a yield above 90% of the theoretical.

TABLE 1

Expt. No.	Amount: 2,2'-dimethoxydiphenylurea (g)	Amount: nitric acid (ml)	Nitric acid concentration (%)	Temperature	Length of time held at the given temperature	Experimental results: yield (g)	yield (%)	melting point of the product
a) Influence of the quantity of nitric acid								
1	10	150	30	80*	3	11.99	89.5	268*
2	10	100	30	80	3	11.90	88.8	273.5
3	10	75	30	80	3	12.10	90.3	269
4	10	75	30	80	3	12.40	93.0	270
5	10	50	30	80	3	12.26	91.5	267
b) Influence of the nitration temperature								
6	10	75	30	100	3	11.05	82.4	273.5
7	10	75	30	95	3	11.75	87.4	272
8	10	75	30	90	3	11.78	87.9	272
9	10	75	30	80	3	12.21	91.3	269
10	10	75	30	80	3	12.30	92.4	270
11	10	75	30	70	3	12.1	90.3	265
c) Influence of the length of the holding at the given temperature								
12	10	75	30	80	2	12.22	91.1	268
13	10	75	30	80	3	12.60	93.3	271
14	10	75	30	80	3	12.49	93.5	270
15	10	75	30	80	4	12.09	90.2	269
16	10	75	30	80	6	11.75	87.6	272
17	10	75	30	80	8	11.73	87.5	270
d) Influence of the nitric acid concentration								
18	10	75	40	80	3	11.85	88.4	265
19	10	75	30	80	3	11.93	89.0	270
20	10	75	20	80	3	12.08	90.1	270
21	10	75	15	80	3	12.50	93.2	268
22	10	75	15	80	3	12.48	93.1	265
23	10	75	10	80	3	12.00	89.5	260
24	30	225	15	80	3	36.75	91.8	275

Hydrolysis in a pure water medium, without addition of ammonia, also gives a high yield of the end product, but it is qualitatively poorer, since some resinification occurs in this case.

The quality of the p-nitro-o-anisidine is considerably improved by purifying the crude product with the aid of sulfuric acid; the losses during this purification amount to about 3%.

We assume, however, that the necessity for such purification may be eliminated, if the end product is isolated not in the form of azoamine, but in the form of its stable diazo compound; the synthesis of p-nitro-o-anisidine via diarylurea and its dinitro-derivative would then be still simpler.

EXPERIMENTAL

Phosgenation of o-anisidine. 30.8 g of o-anisidine and 250 ml of water were placed in a 600 ml four-necked flask, equipped with a stirrer, thermometer, inlet tube for phosgene and outflow tube for the outgoing gases, and then 12.4 g of gaseous phosgene was introduced into the stirred liquid at 25° over a period of 30 minutes. The reaction medium was kept weakly alkaline during the phosgenation by periodic addition of sodium bicarbonate solution. Upon completion of the passage of phosgene, the reaction mixture was stirred for 15 minutes, after which air was blown through to eliminate the excess phsogene and the mixture was filtered. The filtered product was washed several times with weak hydrochloric acid, pressed out well and dried at 60-80°. The dry crystalline product had a light grey color.

A total of about 1% of o-anisidine which had not reacted was contained in the filtrate and the wash water. The yield of 2,2'-dimethoxydiphenylurea was 98.5-98.8% of the theoretical; the m.p. was 183°. After recrystallization from chlorobenzene, the m.p. was 185-185.5°, which was in accord with that indicated in the literature.

Nitration of 2,2'-dimethoxydiphenylurea. Nitric acid was introduced into a 200 ml three-necked flask equipped with a stirrer, a thermometer and a reflux condenser, and while the stirrer was going, a paste of 2,2'-dimethoxydiphenylurea in a quantity which was equivalent to 10 g of the dry substance with a m.p. of 183-185°, was placed in the flask. The mixture was heated to 80° and held at this temperature for 3 hours. Insignificant quantities of the anti-foaming agent acidol or the anti-foaming agent OP-7 and OP-10 (by-products of the soap industry) were added in separate experiments. The mixture was then cooled to 40-45° and filtered off. The 4,4'-dinitro-2,2'-dimethoxydiphenylurea was washed with cold water until the wash water was no longer acid to Congo red, was pressed out well and dried at 100°.

The influence of the quantity and concentration of the nitric acid, the influence of the temperature and the duration of the reaction (at 80°) are presented in Table 1.

4,4'-Dinitro-2,2'-dimethoxydiphenylurea was purified with the aid of glacial acetic acid and chlorobenzene; the m.p. was 280° (in bulk).

Hydrolysis of 4,4'-dinitro-2,2'-dimethoxydiphenylurea. 36.2 g of 4,4'-dinitro-2,2'-dimethoxydiphenylurea (0.1 mole) in the form of a paste and as much aqueous ammonia solution as was necessary for the total ammonia concentration (taking into account the water included in the paste) to amount to 7%, while its quantity was 1,000 ml, were placed in a 8-liter, enameled autoclave equipped with an ammonia manometer, a stirrer and a socket for the thermometer.

The autoclave was closed, the mixture stirred, and then, with the stirrer stopped, was heated for 3 hours at 150°; the pressure reached 9-10 mm. After cooling the autoclave, its contents were filtered; the precipitate was washed with water, pressed out and dried at 80°. The yield of dry 2-methoxy-4-nitroaniline was 28.3 g (84%); the m.p. was 136-137°.

Purification of 2-methoxy-4-nitroaniline. A well-pressed-out paste of 2-methoxy-4-nitroaniline, which contained 28.3 g of the dry product, was placed in a porcelain beaker, 220 g of 35% sulfuric acid was added and the mixture was heated for 20 minutes at 100° while being stirred. The hot acidic solution was filtered and about 150 ml of water was preliminarily poured into the suction flask. The insoluble residue was washed on the filter

TABLE 2

Expt. No.	Amount: dinitro product (g)	Amount: aqueous ammonia solution (ml)	Concentration of the aqueous ammonia solution (%)	Experimental results: yield (g)	yield (%)	m.p. of the product	yield of the final product after purification (g)	(%)	m.p. of the final product
1	36.2	1000	7	28.3	84.0	136°	27.15	80.6	139°
2	30	900	4.5	23.66	84.2	136.5	22.5	80.7	139.5
3	30	900	1	25.85	90.1	135	24.69	86.6	139
4	20	800	1	17.7	93.0	134.5	16.96	90.2	138
5	30	900	9	22.3	80.2	137	21.86	78.6	140

with hot water (2 times with 50 ml portions). The purified 2-methoxy-4-nitroaniline, which precipitated from the cooled filtrate, was filtered off, washed with cold water until the wash water no longer had an acid reaction, and was dried at 80° The weight of the dry 2-methoxy-4-nitroaniline was 27.15 g (80.6%); m.p. 139-140°.

The results obtained in the experiments with aqueous ammonia solutions of various concentrations, are presented in Table 2.

4,4'-Dinitro-2,2'-dimethoxydiphenylurea was hydrolyzed in an aqueous medium in the same autoclave. 161 g of 4,4'-dinitro-2,2'-dimethoxydiphenylurea in the form of a paste (50 g of the dry product) and 389 ml of water were placed in an autoclave so that the total quantity amounted to 500 ml. The mixture was heated to 160° while being stirred and held at this temperature for 3 hours. The maximum yield of 2-methoxy-4-nitroaniline was 91.4% of the theoretical (m.p. 130°). After purification by dissolving it in 10% hydrochloric acid and precipitation with calcined soda, the yield of 2-methoxy-4-nitroaniline amounted to 86% (m.p. 135°).

SUMMARY

1. A new method proposed by us for the synthesis of 2-methoxy-4-nitroaniline via the diarlyurea and its dinitro-derivative has advantages over the method currently used in industry.

2. The treatment of o-anisidine with phosgene readily leads to the formation of 2,2'-dimethoxydiphenylurea.

3. The method of preparing the dinitro-derivatives of diphenylurea by the action of dilute nitric acid at increased temperature was also found entirely applicable for the nitration of 2,2'-dimethoxydiphenylurea.

4. The hydrolysis of 4,4'-dinitro-2,2'-dimethoxydiphenylurea proceeds readily in a 1% aqueous solution of ammonia at increased temperature and pressure.

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* See Consultants Bureau Translation, page 1419.

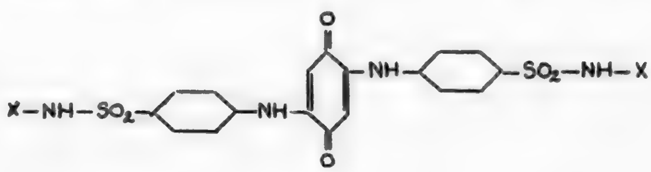
** See Consultants Bureau Translation, pages 1637, 2259.

INVESTIGATION IN THE FIELD OF QUINONES

VIII [1]. CONDENSATION OF p-BENZOQUINONE WITH SULFANILAMIDES

I. S. Ioffe, N. A. Filippova and Z. Ya. Khavin

In 1946 Postovsky and Pushkareva [2] described the products of the condensation of p-benzoquinone and chloranil with sulfanilamide and with sulfanilacetamide, which contain, joined with the quinoid nucleus, 2 sulfanilamide radicals, of the general type (I):



(I)

In developing this work, we condensed p-benzoquinone with sulfapyridine, sulfathiazole and sulfapyrimidine and thereby obtained the correspondingly amino group-substituted derivatives of the disulfanilamidoquinone type (I).

Like unsubstituted disulfanilamidoquinone, all the substances obtained were insoluble in water and in ordinary organic solvents. They melt above 300°. For purification we subsequently boiled the reaction products with alcohol and with acetic acid until colorless filtrates were obtained. To analyze them for sulfur content, we used the method of oxidizing with permanganate in an alkaline solution with subsequent reduction of the excess permanganate with hydrochloric acid and precipitation of the sulfate ion in the form of barium sulfate. This method, among other things, is entirely applicable for the analysis of various sulfanilamides.

The disulfanilamidoquinones were soluble in dilute aqueous solutions of caustic alkalis, but were not dissolved even in 10% soda. The alkaline solutions of the disulfanilamidoquinones were brown colored, and upon acidification, unchanged disulfanilamidoquinones were recovered from them. Reprecipitation from alkali is also applicable for purifying these substances.

However, when alkaline solutions of the sulfanilamidoquinones are kept for a long time, the latter, even at room temperature, are slowly decomposed. Thus, for example, when 1 g of distreptocidoquinone was dissolved in 200 ml of 0.1 N NaOH and the solution obtained was acidified, 0.8 g of unchanged starting material was recovered after keeping the solution at room temperature for 4 hours; but after keeping such a solution for several days no precipitate of distreptocidoquinone whatever was isolated upon acidification. Distreptocidoquinone is least stable in alkaline solutions. The presence, in the amide groups of the sulfanilamidoquinones, of heterocyclic radicals increases their stability to alkalis. The most stable is disulfapyrimidinoquinone.

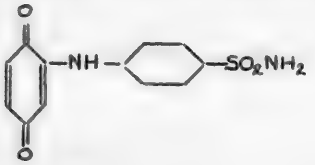
In view of the practical insolubility of the disulfanilamidoquinones, we decided to prepare the hitherto unknown monosulfanilamidoquinones, expecting that they would be distinguished by a better solubility in organic solvents.

Diamino derivatives are ordinarily formed by the reaction of p-benzoquinone with amino compounds. However, diverse monoaminoquinones have been described in the literature, for example, monoanilinoquinone [3, 4] and mono-(methylamino)-quinone [4]; we have prepared monoglycinoquinone and monoalaninoquinone [5].

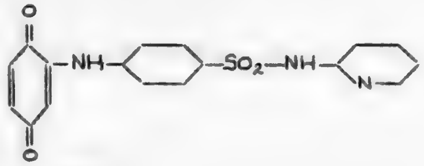
There are indications [3] that it is easier to stop the reaction at the monoaminoquinone stage when slightly active amines are acting on the quinone. We assumed that the formation of monoaminoquinones must be facilitated by the presence in the reaction medium of excess quinone, and the conduct of the reaction under conditions in which the monoamino derivative settles out as a precipitate as it is formed. On these grounds, we carried out the reaction of p-benzoquinone with sulfanilamide in a dilute aqueous solution in the presence of sodium chloride at ordinary temperature and introduced a considerable excess of quinone (from 6 to 10 moles per mole of amine) into the reaction. The gradual settling out of a reddish-brown flocculent precipitate, which consisted of a mixture of

disulfanilamidoquinone and monosulfanilamidoquinone with a considerable predominance of the latter, was thereupon observed.

We treated the mixture obtained with boiling alcohol to separate the monosulfanilamidoquinone, filtered the solution from the alcohol-insoluble distreptocidoquinone and then diluted the alcoholic solution with water and thus isolated the monostreptocidoquinone (II):



(II)



(III)

We prepared monosulfidinoquinone (III) analogously.

Monosulfanilamidoquinones are quite soluble in alcohol and in acetic acid and can be isolated from these solvents by precipitation with water. However, when the filtered alcohol or acetic acid solutions of monosulfanilamidoquinone are let stand, and especially when they are boiled, a precipitate is gradually formed which is still insoluble in alcohol and in acetic acid. In exactly the same way, in an attempt to recrystallize monosulfanilamidoquinone from the filtered concentrated solutions in alcohol or in acetic acid, a substance was isolated which was only partially soluble in these solvents.

This can be explained by the probable conversions of the monoamino derivative, which contains active carbonyl groups and an unsubstituted hydrogen atom on the amine nitrogen and is, consequently, capable of polymerization with the formation of polymers which are distinguished by poorer solubility in organic solvents. The tendency of monoaminoquinones toward polymerization was noted rather long ago [6].

EXPERIMENTAL

Disulfanilamidoquinones

2,5-Disulfapyridinobenzoquinone. We dissolved 2.5 g (0.01 mole) of sulfidine by heating it with a reflux condenser in 100 ml of alcohol and added a solution of 2.2 g (0.02 mole) of benzoquinone in 100 ml of hot water to the solution obtained, which was being stirred. The mixture acquired a red color and a light brown precipitate quickly settled out. The mixture was stirred and boiled for 3 hours. The precipitate was filtered off and washed with alcohol. We boiled it in a flask with a reflux condenser in 150 ml of 80% acetic acid to purify it. After cooling, the precipitate was filtered off and repeatedly washed with hot acetic acid. The yield was 2.68 g.

0.1132, 0.1157 g sub.: 0.0897, 0.0893 g $BaSO_4$. Found %: S 10.85, 10.58. $C_{28}H_{22}O_6N_6S_2$. Calculated %: S 10.69.

2,5-Disulfathiazolobenzoquinone. 2.5 g (0.01 mole) of sulfathiazole was dissolved by heating on a water bath with a reflux condenser in 100 ml of alcohol, to which we added 200 ml of water. When all the substance had dissolved, 2.2 g (0.02 mole) of benzoquinone was added to the solution and the heating was continued for 3 hours more while the solution was stirred. The precipitate was filtered off and washed with hot water. It was then treated several times with 80% acetic acid in a flask with a reflux condenser, and dried. The yield was 2.65 g.

0.1281, 0.1227 g sub.: 0.1904, 0.1826 g $BaSO_4$. Found %: S 20.36, 20.38. $C_{24}H_{18}O_6N_6S_4$. Calculated %: S 20.91.

2,5-Disulfapyrimidinobenzoquinone. We dissolved 2.5 g (0.01 mole) of sulfapyrimidine in 100 ml of alcohol in a flask with a reflux condenser. 2.2 g (0.02 mole) of benzoquinone was added to the solution which still contained a small quantity of undissolved sulfapyrimidine and the heating was continued for 5 hours more while the mixture was being stirred. The dark brown precipitate was filtered off, washed with hot water and treated several times with boiling 50% acetic acid in a flask with a reflux condenser and dried. The yield was 2.3 g.

0.1387, 0.1163 g sub.: 0.1077, 0.0922 g $BaSO_4$. Found %: S 10.61, 10.86. $C_{26}H_{20}O_6N_8S_2$. Calculated %: S 10.59.

Monosulfanilamidoquinones

Sulfanilamidobenzoquinone. 43 g (0.4 mole) of the benzoquinone was dissolved in 2 liters of water heated to 60° and poured while being stirred into a flask which contained 3.5 liters of cold water and 0.5 liters of saturated

NaCl solution. When the solution obtained had come to room temperature, a hot solution of 9 g (0.05 mole) of streptocidin in 100 ml of alcohol was poured into it while it was being stirred. A flocculent cherry-red precipitate settled out of the mixture, which had become red. After three days, the precipitate was filtered off, washed with water and dried in air. It was then twice treated, in a flask with a reflux condenser, with boiling alcohol in portions of 200 and 100 ml, and each time the insoluble residue from the filtration was washed with alcohol.

5 g of alcohol-insoluble residue of disulfanilamidoquinone was obtained. The combined alcoholic solution after the repeated filtration was diluted with water, which contained 10% sodium chloride for better coagulation of the precipitate. The precipitate of monosulfanilamidoquinone which was formed was filtered off, washed with water and dried. The yield was 7.6 g. The monosulfanilamidoquinone was again reprecipitated from alcohol for purification.

0.1115, 0.1405 g sub.: 0.0860, 0.1088 g $BaSO_4$. Found %: S 10.58, 10.60. $C_{12}H_{10}O_4N_2S$. Calculated %: S 11.51.

Sulfapyridinoquinone. 5 g (0.02 mole) of sulfidine was dissolved in 100 ml of alcohol by boiling in a flask with a reflux condenser and the hot solution obtained was poured into a flask containing 3 liters of water and 1 liter of a saturated NaCl solution. After stirring, 15 g (0.14 mole) of a solution of benzoquinone in 1 liter of hot water was added to it and the volume of the solution was brought with water to 6 liters. After 3 days the precipitate was filtered off, washed with water and dried. It was then twice treated in a flask with a reflux condenser with boiling 96% acetic acid in 200 and 100 ml portions, filtered off and washed with acetic acid. After drying, 1.5 g of disulfapyrimidinoquinone was obtained.

The combined acetic acid solution was filtered once more and diluted with a large quantity of water. Brown flakes of monosulfapyridinoquinone thereupon precipitated and were filtered off, washed well with water and dried. The yield was 3.4 g. The monosulfapyridinoquinone was again reprecipitated from 96% acetic acid for purification.

0.1197, 0.1204 g sub.: 0.0791, 0.0794 g $BaSO_4$. Found %: S 9.07, 9.80. $C_{17}H_{13}O_4N_3S$. Calculated %: S 9.01.

SUMMARY

The preparation of disulfapyridinoquinone, disulfathiazoloquinone and disulfapyrimidinoquinone, and also of monosulfanilamidoquinone and monosulfapyridinoquinone was described.

In contrast to the disulfanilamidoquinones, the monosulfanilamidoquinones are quite soluble in alcohol and in acetic acid. When such solutions are let stand and particularly when they are heated, the monosulfanilamidoquinones are gradually converted into insoluble substances which are probably polymerization products.

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** See Consultants Bureau Translation, page 533.

INVESTIGATION IN THE FIELD OF QUINONES

IX [1]. REACTION OF METHOXYQUINONES WITH AMINES

I. S. Ioffe and A. F. Sukhina

The influence of the methoxy group on the course of a process was established in the study of the chlorination of methoxyquinones [2]. We decided to study the influence of the methoxy group on the reaction of quinones with amines, and, in particular, with aniline and with certain sulfanilamides.

When an alcoholic solution of aniline and methoxyquinone (I) is heated with an excess of the latter, the solution becomes raspberry colored. Upon cooling the solution, the reaction product crystallizes in the form of dark red needles with a constant m.p. of 160°. Analytical determinations showed that the molecule of the compound being formed contains 1 methoxy group and 1 phenylamino group. The distribution of these groups with respect to each other remained unknown. The following observation assisted in the solution of the problem: on heating an alcoholic solution of the starting materials with excess aniline, the raspberry color which initially appeared quickly disappears and another reaction product precipitates from the solution, which is not soluble in alcohol and, as regards the manner of its formation, is evolved in the form of red crystalline spangles. This substances proved to be identical with the dianilinoquinone (III) which was obtained for the first time as early as 1863 [3] by heating aniline with p-benzoquinone (IV). Dianilinoquinone is formed by heating aniline and the above-described methoxyanilinoquinone with a m.p. of 160°. It follows from this that, in this compound, the methoxy and phenylamino groups are located in the para-position to each other (II).

The substance, to which was ascribed the structure of 2-methoxy-5-anilinoquinone (II), was described in the literature [4] as having the form of brown needles with a m.p. of 189°. However, this substance was not obtained via the reaction of methoxyquinone with aniline, but by a roundabout route from 2-hydroxy-5-anilinoquinonanil, by heating the latter with methyl alcohol and strong sulfuric acid. The use in the concluding stage of strong sulfuric acid which has so energetic an action on quinones, raises doubt as to the degree of purity or as to the correctness of the structure of the substance obtained under these conditions. Our experiments showed that 2-methoxy-5-anilinoquinone has a dark red color and melts sharply at 160°.

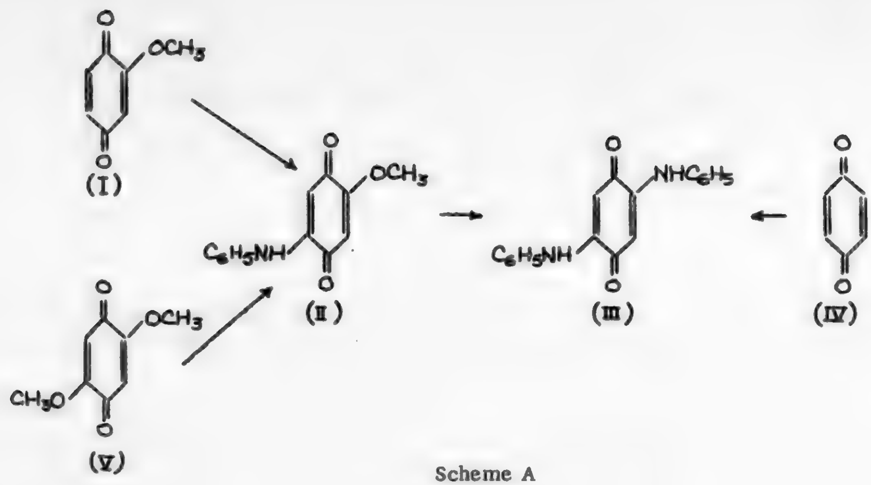
The experiments described above show that, in the reaction of methoxyquinone with amines, the former initially adds one amino radical in the para position to the methoxy group, and then, in the presence of excess amine, the replacement of the methoxy group by another amino radical occurs.

In view of this, we decided to study the reaction between amines and 2,5-dimethoxyquinone (V). It turned out that when 2,5-dimethoxyquinone is heated with aniline in the presence or in the absence of solvents, 2,5-dianilinoquinone is also formed. In contrast to the other substituted quinones, 2,5-dimethoxyquinone reacts with amines only with replacement of the methoxy groups by amine radicals. It also proved possible to carry out this replacement in stages. Upon heating a solution of 2,5-dimethoxyquinone in glacial acetic acid with a small quantity of aniline (1 mole of aniline per 2 moles of dimethoxyquinone), the solution becomes red colored and a dark red precipitate is formed from the solution upon dilution which, after crystallization, was identified as 2-methoxy-5-anilinoquinone.

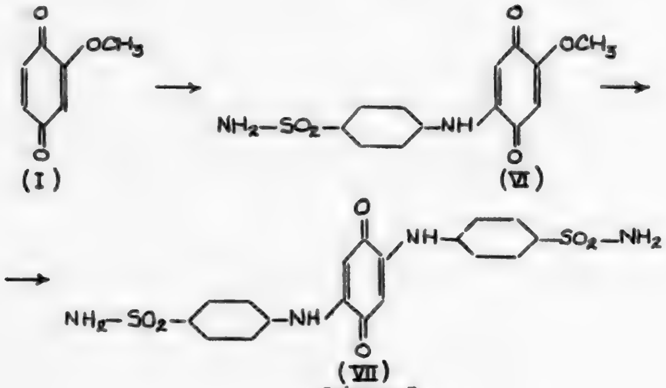
The transformations of methoxyquinone and 2,5-dimethoxyquinone studied by us can be represented by Scheme A.:

We obtained analogous results in the reaction of methoxyquinone (I) with sulfanilamide. On heating an alcoholic solution of a mixture of substances with excess quinone, 2-methoxy-5-sulfanilamidoquinone (VI), which crystallizes from glacial acetic acid in the form of reddish-brown prisms with a m.p. of 279-280°, is formed. On heating this substance with sulfanilamide or on heating an alcoholic solution of methoxyquinone and sulfanilamide with an excess of the latter, the fine spangles of disulfanilamidoquinone (VII), previously described by Postovsky and Pushkareva [5] precipitate. (See Scheme B.)

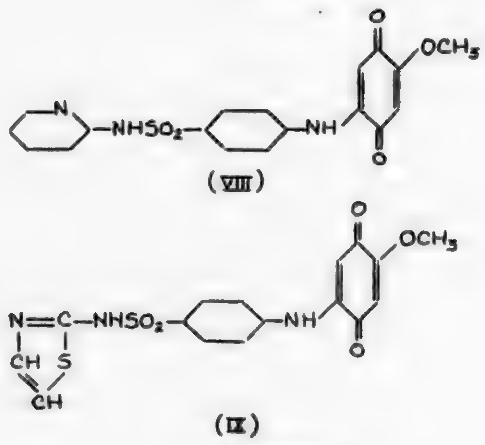
When we carried out this methoxyquinone reaction with sulfapyridine and sulfathiazole, we obtained, respectively, 2-methoxy-5-sulfapyridinoquinone (VIII) and 2-methoxy-5-sulfathiazoloquinone (IX), which melted at 273° and 245°. (See Scheme C.)



Scheme A



Scheme B



Scheme C

The experiments which were performed show that the reaction of methoxyquinones with amines proceeds in two directions: with the addition of the amino radical to the unsubstituted carbon atom of the quinone nucleus in one direction; and with replacement of the methoxy group by the amino group in the other. Under the influence of the methoxy group, the amino radical initially, and with greater speed, adds to the unsaturated carbon atom of the quinoid nucleus, necessarily in the para-position to the methoxy group. With excess amine, even under the influence of the available amino group, the methoxy group in the para-position to the latter is replaced by a second amino radical and the reaction is concluded at this point. In the 2,5-dimethoxyquinone, in which both

methoxy groups are located in the para-position to each other, replacement of these groups by the amino radicals is still possible and proceeds in stages.

The experimental facts presented in a recently published work [6], are in complete accord with these conclusions; it was shown in this work that on heating either methoxyquinone or 2,5-dimethoxyquinone with excess methylamine, 2,5-di-(methylamino)-quinone is formed. 6-Methoxy-2,5-di-(methylamino)-quinone was not obtained from the 2,6-dimethoxyquinone. These data confirm that the reaction of methoxyquinones with amines proceeds in the two directions indicated above. The authors of the work cited did not analyze both these directions and, consequently, did not establish the laws governing the present reaction.

EXPERIMENTAL

Reaction of Methoxyquinone with Aniline

Preparation of 2-methoxy-5-anilinoquinone. 5 g (2 moles) of methoxyquinone was heated with 75 ml of alcohol until it was completely dissolved. 1.5 g (1 mole) of aniline was added to the boiling solution and it was boiled for 2 hours on a water bath. After cooling, a precipitate in the form of fine dark red needles settled out from the dark red solution.

The precipitate was filtered off, washed with a small quantity of alcohol and dried over calcium chloride. The weight of the precipitate was 3.5 g. After 2-fold crystallization from 50% aqueous alcohol, long dark red needles with a m.p. of 160° were obtained. This substance was moderately soluble in water, and soluble in alcohol, benzene and toluene.

0.1271, 0.1240 g sub.: 0.1316, 0.1285 g AgI (Zeisel). 0.1742, 0.1576 g sub.: 7.88, 7.00 ml 0.1 N H_2SO_4 (Kjeldahl). Found %: OCH_3 13.68, 13.68; N 6.31, 6.22. $C_{13}H_{11}O_3N$. Calculated %: OCH_3 13.54; N 6.57.

Preparation of dianilinoquinone. a) From 2-methoxy-5-anilinoquinone. 1 g of 2-methoxy-5-anilinoquinone was dissolved in 50 ml of boiling acetic acid and 1 g of aniline was added. Precipitation thereupon began. The solution was boiled for 2 hours and was again filtered while hot. The precipitate which settled out in the form of spangles (1.2 g) was not soluble in alcohol or acetic acid and crystallized from nitrobenzene. Shiny dark red flakes, identified as 2,5-dianilinoquinone, were obtained; the melting point was above 300°. The analytical determinations demonstrated the complete absence of methoxy groups.

b) From methoxyquinone. 5 g (1 mole) of methoxyquinone was dissolved in 75 ml of boiling alcohol and 8.5 g of aniline (2.5 moles) was added. After boiling for 2 hours, the precipitate of 2,5-dianilinoquinone was filtered off from the hot solution. Its weight was 6 g.

Reaction of Methoxyquinone with Sulfanilamide

5 g (2 moles) of methoxyquinone was dissolved in 75 ml of boiling alcohol and 2.5 g (1 mole) of sulfanilamide was added to the boiling solution. The solution obtained was boiled for 2 hours and after cooling, the precipitate which settled out was filtered off. Its weight was 3 g. After 3-fold crystallization from glacial acetic acid, fine reddish-brown prisms with a m.p. of 279-280° were obtained. The substance was weakly soluble in water and was soluble in alcohol and glacial acetic acid. Upon boiling in an acetic acid solution with excess sulfanilamide, it was converted into the disulfanilamidoquinone.

0.1726, 0.1537 g sub.: 0.1320, 0.1190 g AgI (Zeisel). 0.1628, 0.1954 g sub.: 12.15, 14.96 ml 0.1 N H_2SO_4 (Kjeldahl). Found %: OCH_3 10.11, 9.58; N 10.44, 10.70. $C_{13}H_{12}O_5N_2S$. Calculated %: OCH_3 10.07, N 9.1.

Reaction of Methoxyquinone with Sulfidine

5 g (2 moles) of methoxyquinone was dissolved in 75 ml of boiling alcohol and 4 g (1 mole) of sulfidine was added to the boiling solution. The solution obtained was boiled with continuous stirring for 2 hours and after cooling, the light red precipitate which settled out was filtered off. Its weight was 3.5 g.

After 2-fold crystallization from 80% acetic acid, shiny light red petals with a m.p. of 273° (with decomposition) were obtained. The substance was insoluble in water and alcohol. It was soluble in a ratio of 1:250 in 80% acetic acid.

Sulfur determination, by Messinger's method:

0.1543, 0.1372 g sub.: 0.0878, 0.0805 g $BaSO_4$. Found %: S 7.98, 7.75. $C_{18}H_{15}O_5N_3S$. Calculated %: S 8.06.

Reaction of Methoxyquinone with Sulfathiazole

5 g (2 moles) of methoxyquinone were dissolved in 75 ml of boiling alcohol and 4.5 g (1 mole) of sulfathiazole was added to the hot solution. The solution obtained was boiled for 2 hours and after cooling, the precipitate which settled out was filtered off. Its weight was 3 g. After 2-fold crystallization from 60% acetic acid, a finely crystalline Bordeaux red precipitate with a decomposition temperature of 245-247° was obtained. The substance was insoluble in water, benzene and ether and was weakly soluble in alcohol, and soluble in glacial and dilute acetic acid.

Sulfur determination, by Messinger's method:

0.1844, 0.1670 g sub.: 0.2214, 0.1996 g $BaSO_4$. Found %: S 16.33, 16.27. $C_{16}H_{13}O_5N_3S_2$. Calculated %: S 16.36.

Reaction of 2,5-Dimethoxyquinone with Aniline

Preparation of dianilinoquinone. 1 g of 2,5-dimethoxyquinone was dissolved in 75 ml of boiling acetic acid and 1 g of aniline was added. Under these conditions the solution was initially red colored, but spangles of a substance which was insoluble in acetic acid quickly began to precipitate. The mixture was boiled for 2 hours and the precipitate was filtered off from the hot solution. Its weight was 1 g. The reaction product did not contain methoxy groups. After crystallization from nitrobenzene the 2,5-dianilinoquinone was obtained in the form of shiny brown flakes with a melting point above 300°.

Preparation of 2-methoxy-5-anilinoquinone. 1 g of 2,5-dimethoxyquinone (2 moles) was dissolved in 75 ml of boiling acetic acid, 0.3 g of aniline (1 mole) was added and the mixture was boiled for 2 hours. The red solution obtained was concentrated to 10 ml and after cooling was diluted with 90 ml of water; the precipitate which settled out was filtered off. Its weight was 0.8 g. After 3-fold crystallization from 50% aqueous alcohol, dark red needles of a substance with a m.p. of 160° were obtained, which were identified as 2-methoxy-5-anilinoquinone.

SUMMARY

The corresponding 2-methoxy-5-aminoquinones were obtained by the reaction of methoxyquinone with aniline, sulfanilamide, sulfapyridine and sulfathiazole. On treating 2-methoxy-5-phenylaminoquinone with excess aniline, as well as during the direct reaction of methoxyquinone with excess aniline, dianilidoquinone is formed. The same product is obtained by heating aniline and 2,5-dimethoxyquinone together. Analogous results are obtained by heating methoxyquinone with excess sulfanilamide.

The reaction of methoxyquinones with amines proceeds in two directions – in one, with the addition of an amino radical to the unsubstituted carbon atom of the quinoid nucleus, and in the other, with replacement of the methoxy group by an amino group.

Under the influence of the methoxy group, the amino radical adds to the unsubstituted carbon atom, if there is any, at a great rate and in the para-position to the amino group. Replacement of the methoxy group by one more amino radical in the presence of excess aniline still proceeds at lower rate and is necessarily in the para-position to the amino group already present. 2,5-Dimethoxyquinone reacts only with replacement of the methoxy groups and this replacement proceeds in stages.

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* See Consultants Bureau Translation, page 715.

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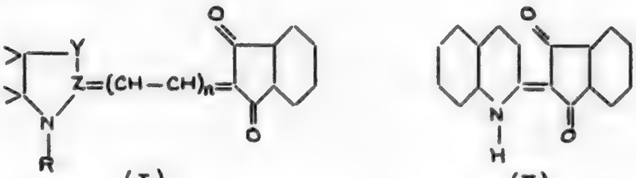
THE COLOR OF CERTAIN MEROCYANIN DYES WHICH ARE DERIVATIVES OF INDANDIONE-1,3

V. G. Zhiryakov and I. I. Levkoev

Mercoyanines, which are derivatives of indandione-1,3 (I) containing an external polymethine chain, have been studied very little [1-4] up to now, although the simplest dyes of this group, which contain the quinoline residue, are known under the name of "quinophthalones"(II) and have been subjected to detailed investigations [5-8]:



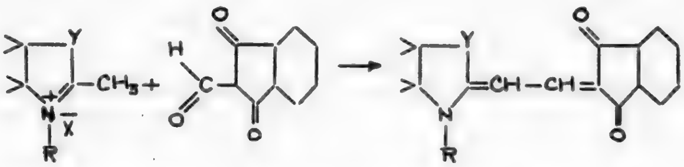
(I) (II)

Ordinary quinophthalones, which contain hydrogen on the nitrogen atom of the heterocyclic radical – the sulfo acids of which are used as yellow acid dyes – have been prepared by the reaction of phthalic anhydride with quinaldine [5]. However, the N-alkyl derivatives of the quinophthabnes [8] are also known.

The merocyanine dyes, which contain the indandione-1,3-radical, are of considerable interest in the study of the relation between color and structure, since due to the presence of two carbonyl groups in them, very considerable electron displacement from the nitrogen atom of the heterocyclic radical is probable, and this has actually been confirmed for a few dimethine dyes of this group [2, 3].

In this connection, we synthesized a number of di-, tetra- and hexamethin-merocyanines – derivatives of indandione-1,3-with the radicals 3,3-dimethylindolenine, benzthiazole and 4,5-diphenylthiazole which have respectively low, average and high basicity; the optical properties of these dyes were studied.

Dimethinmerocyanines with the 3,3-dimethylindolenine, benzthiazole and 4,5-diphenylthiazole radicals were synthesized via the condensation of 2-formyl-3-hydroxyindenone-1 with the quaternary salts of the corresponding 2-methyl-substituted heterocyclic bases by heating with anhydrous ethyl alcohol in the presence of triethylamine:

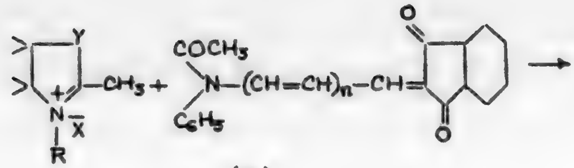


The tetra- and hexamethinmerocyanines were prepared analogously, starting with 2,β-acetanilinoallylidenand pentadienylidenindandione-1,3 (III) (see a).

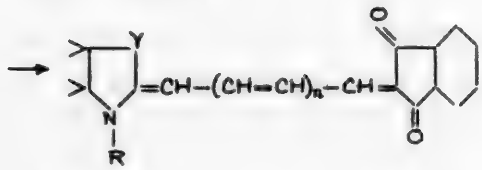
With the object of calculating "hypsochromic displacement" of the absorption maxima of the merocyanines obtained, oxanine dyes were synthesized – derivatives of indandione-1,3 with 3 and 5 methine groups in the external polymethine chain.

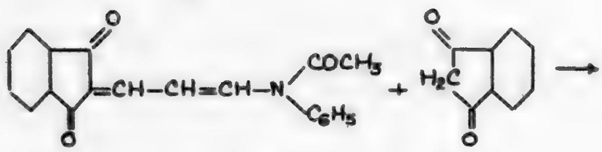
Trimethinoxanine (IV) was prepared by the reaction of 2-β-acetanylinoallylidenindandione-1,3 with indandione-1,3 by heating with anhydrous ethyl alcohol in the presence of triethylamine (see b).

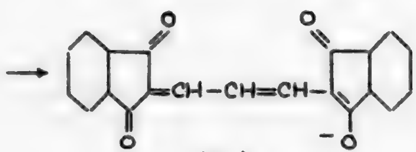
Pentamethinoxanine was successfully prepared by the direct condensation of indandione-1,3 with the hydrochloride of the dianil of glutaconic aldehyde under analogous conditions.

a) 

(III)



b) 



(IV)

The majority of the dyes obtained were chromatographed on active aluminum oxide for purification.

In Table 1 are presented the absorption maxima of the merocyanines obtained, the "hypsochromic displacement" of their absorption maxima in comparison with that calculated for the corresponding symmetric oxanines and cyanines, and also the bathochromic displacement of the absorption maxima caused by lengthening the external polymethine chain by one vinylene group.

The absorption maxima of the salts of the mono-, tri- and pentamethinoxanines — derivatives of indandione-1,3 — lie at 459, 551 and 650 mμ, respectively.

In considering the data presented in Table 1, one's attention is, first of all, attracted to the anomalously small magnitudes of the "hypsochromic displacements" of the absorption maxima of all the di-, tetra- and hexamethinmerocyanines, which are derivatives of indandione-1,3. In addition, the dyes which are derivatives of indandione-1,3, upon elongation of the polymethine chain, in a number of cases form not a congruent, but even a rather divergent series of absorption maxima. An analogous phenomenon has been observed previously to a lesser extent only for certain merocyanines which are derivatives of phenylisoxazolone [2].

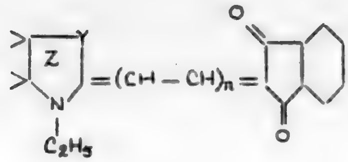
The very insignificant "hypsochromic displacement " of the absorption maxima in the dyes which are derivatives of indandione-1,3, and also the formation of a rather divergent series of values of the absorption maxima formed on elongating their external polymethine chain, compels us to assume that in such dyes the electron displacement from the nitrogen atom of the heterocyclic residue is very great. As a result of such displacements, in the majority of such dyes, evidently, a comparatively regular distribution of the electron density in the polymethine chromophore is brought about and is chiefly responsible for their deep color.

The position of the absorption maxima of the merocyanine dyes, which are derivatives of indandione-1,3, in solvents of varying polarities was measured with the object of confirming these assumptions. Such measurements, to elucidate the character of the distribution of the electron density in the molecules of the merocyanine dyes, are usually carried out in several different solvents [9, 10]. As a rule, methyl or ethyl alcohol, benzene, chloroform, etc. are used for this purpose.

This method has a substantial disadvantage that consists in the fact that it is impossible to use it to regularly proceed from a less polar to a more polar solvent; this is of great importance in this kind of investigations.

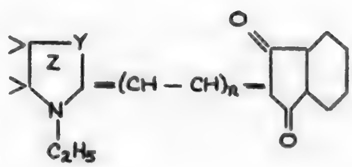
A large number of other factors besides the dielectric constant of the solvent influence the structure and, consequently, the position of the absorption maximum of the merocyanine (for example, the possibility of the

TABLE 1



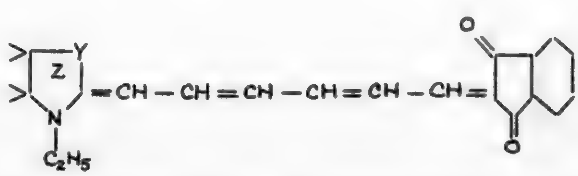
Z	n	Absorption maximum in ethyl alcohol (in mμ)		Vinylenic displacement of the absorption maximum (in mμ)	Hypsochromic displacement (in mμ)
		of the corresponding cyanine	observed for the merocyanine		
3,3-Dimethylindolenine	1	546	495	–	7.5
	2	634	588	93	4.5
	3	746	684	96	14.0
Benzthiazole.	1 [1]	558	506	–	2.5
	2	654	596	92	4.5
	3	763	706	108	0.5
4,5-Diphenylthiazole . .	1	588	520	–	3.5
	2	683	611	91	6.0
	3	–	722	111	–

TABLE 2



Z	n	Absorption maximum (in mμ)							
		percent content by weight of n-decyl alcohol in the mixture							in ethyl alcohol
		0	20	40	60	80	90	100	
3,3-Dimethylindolenine	1	493	–	–	495	495	–	495	495
	2	584	584	586	588	588	586	586	588
Benzthiazole	1	502	–	505	507	–	–	509	506
	2	594	597	600	601	603	603	602	598
4,5-Diphenylthiazole . .	1	516	–	–	520	522	–	525	520
	2	605	608	–	615	617	–	620	611

TABLE 3



Z	Absorption maximum (mμ)				
	percent content by weight of n-decyl alcohol in the mixture				in ethyl alcohol
	0	40	60	100	
3,3-Dimethylindolenine	686	684	683	675	684
Benzthiazole.	706	706	706	705	706
4,5-Diphenylthiazole . .	714	724	732	738	722

formation of hydrogen bonds, the dipole moment and others); these depend on the chemical nature of the solvents used and, consequently, the use of solvents which are markedly different from each other in their nature, is also a rather considerable defect in the method described above. L. Brooker and his coworkers in their latest work [2-4] have eliminated the first of these deflects by using for this sort of investigation mixtures of pyridine and water, which vary considerably in their polarity; the percentage content of pyridine in the mixtures is varied gradually which made it possible to regularly change the polarity of the solvent. However, the second defect, to wit, the marked difference in the chemical nature of the solvents used, still remains in this work, which does not make is possible to consider the results obtained by these authors as entirely reliable.*

We selected methyl and n-decyl alcohols and their mixtures to obtain more precise results in the investigation of the structure of the dyes which are derivatives of indandione-1,3 in solvents of varying polarity. These alcohols were used as solvents because they are representatives of the same homologous series, have approximately equal dipole moments (1.69 and 1.63), but markedly differ in the magnitude of their dielectric constants.

The results of these measurements, for di-, tetra- and hexamethinmerocyanine dyes which are derivatives of indandione-1,3, are presented in Tables 2 and 3.

It is evident from consideration of Table 2 that the color of di- and tetramethinmerocyanines with 3,3-dimethylindolenine radicals remains practically unchanged with change in the polarity of the solvent. It can be supposed that there is a comparatively regular distribution of the electron density along the polymethine chain in the molecules of these dyes or that their structure is insignificantly displaced toward that of an internal-ionic structure.

Di- and tetramethinmerocyanines with benzthiazole and 4,5-diphenylthiazole radicals have an appreciably deeper color (7-15 mμ) with diminishing polarity of the solvent. Evidently, the structure of their molecules in methanol is displaced toward that of the internal-ionic structure, and the irregularity in the distribution of the electron density along the chain is intensified as the basicity of the heterocyclic radical is increased.

Hexamethinmerocyanine with a 3,3-dimethylindolenine radical, as is evident from the data of Table 3, increases its color as one proceeds to less polar solvents. Apparently, the structure of a molecule of this dye even in methanol is displaced toward a covalent structure. In the case of the hexamethine dye with a benzthiazole radical, the color remains practically unchanged as the polarity of the solvent is diminished.

Evidently, the distribution of the electron density in the chromophore of this dye is comparatively regular. The absorption maximum of hexamethinmerocyanine with a 4,5-diphenylthiazole radical is displaced into the short wave portion of the spectrum with increasing polarity of the solvent. The structure of this dye evidently remains displaced toward that of the internal-ionic in all the solvents investigated.

The experiments which were carried out show that for the dyes which are derivatives of indandione-1,3, the relationship between their color and structure is basically the same as for merocyanines with radicals of other ketomethylenic compounds. However, the structure of the majority of them, particularly those with a short polymethine chain, is more correctly depicted by the internal-ionic formula. With lengthening of the chain of these merocyanines, the structure of their molecules is gradually displaced toward a covalent structure, the more rapidly, the less basic the nitrogenous heterocyclic radical which is included in the dye molecule. In general, however, as regards dyes which are similar to merocyanines, the derivatives of the majority of other ketomethylenic compounds are characterized by considerable stability relative to the regular distribution of the electron density in the polymethine chromophore and lowering of the polarity. The latter apparently gradually increases with lengthening of the chain of such merocyanines.

EXPERIMENTAL

1. Intermediate Products

2-(Anilinoallyliden)-indandione-1,3. 4.38 g of indandione-1,3 and 7.75 g of the hydrochloride of the dianil of malonic aldehyde were dissolved in 60.0 ml of anhydrous ethyl alcohol in a flask with a reflux condenser, and 3.0 g of triethylamine was added to the solution. The mixture was heated for 30 minutes on a boiling water bath. After cooling, the precipitate which settled out was filtered off, washed with ethyl alcohol and dried. The yield was 5.7 g (69.2%); m.p. 239-240°. After crystallization from ethyl alcohol, 5.1 g of a substance in the form of dark red needles with a m.p. of 242-243° was obtained. There was an absorption maximum at 580 mμ (in ethyl alcohol).

* It is necessary to mention that L. Brooker and his coworkers tried to explain a portion of his experimental data from the point of view of the basically faulty "theory of resonance".

Found %: N 5.15. $C_{18}H_{13}O_2N$. Calculated %: N 5.09.

2-(Acetanilinoallyliden)-indandione-1,3 was prepared by acetylating the preceding compound (5.1 g) with acetic anhydride (30.0 ml) in the presence of triethylamine (2.1 g) while the solution was being boiled (25 minutes). The precipitate which settled out on cooling was filtered off, washed with water and ethyl alcohol, and dried. The yield was 76.6%. It consisted of dark yellow needles with a m.p. of 244-245° (from ethyl alcohol).

Found %: N 4.51. $C_{20}H_{15}O_3N$. Calculated %: N 4.42.

2-(Anilinopentadienyliden)-indandione-1,3. 1.46 g of indandione-1,3 and 2.84 g of the chloride of the dianil of glutaconic aldehyde were dissolved by heating in 25.0 ml of anhydrous ethyl alcohol, and 1.01 g of triethylamine was added to the solution; an intense dark blue color thereupon appeared and a precipitate began to settle out. The mixture was heated for 20 minutes on a boiling water bath. After cooling, the precipitate was filtered off, carefully washed with ethyl alcohol and acetone until the filtrate had a pure violet color, and dried. The yield was 1.75 g (58.2%), m.p. 189-190°. After crystallization from benzene, 1.38 g of a substance in the form of dark violet needles with a m.p. of 193-194° was obtained. There was an absorption maximum at 560 mμ (in ethyl alcohol).

Found %: N 4.80. $C_{20}H_{15}O_2N$. Calculated %: N 4.65.

2-(Acetanilinopentadienyliden)-indandione-1,3 was synthesized by acetylating the preceding compound (1.75 g) with acetic anhydride (5.0 ml) in the presence of triethylamine (0.58 g) while the solution was being boiled (10 minutes). The precipitate which settled out after cooling was filtered off, washed with water and ethyl alcohol and dried. The yield was 78.8%. It consisted of fine light brown needles with a m.p. of 237-238° (from benzene).

Found %: N 4.25. $C_{22}H_{17}O_3N$. Calculated %: N 4.08.

2. Dyes

2-(1'-Ethyl-3',3'-dimethylindolinyliden-2'-ethyliden)-indandione-1,3

0.16 g of 2,3,3-trimethylindolenine and 0.16 g of diethyl sulfate were heated in a flask with a reflux condenser on a water bath at 80° for 60 minutes. After cooling, the quaternary salt was dissolved by heating it in 4.0 ml of anhydrous ethyl alcohol, and 0.17 g of 2-formyl-3-hydroxyindenone-1 and 0.1 g of triethylamine were introduced into the solution. The liquid was heated on a boiling water bath for 15 minutes.

After cooling, the precipitated dye was filtered off, washed with ethyl alcohol and dried. The yield was 0.14 g (40.8%), m.p. 201-203°.

Found %: N 4.12. $C_{23}H_{11}O_2N$. Calculated %: N 4.08.

2-(3'-Ethyl-4',5'-diphenylthiazolinyliden-2'-ethyliden)-indandione-1,3

0.41 g of the iodoethylate of 2-methyl-4,5-diphenylthiazole and 0.17 g of 2-formyl-3-hydroxyindenone-1 were dissolved in 4.0 ml of anhydrous ethanol in a flask with a reflux condenser. 0.11 g of triethylamine was introduced into the solution and a dark red color appeared at once. The liquid was heated on a boiling water bath for 15 minutes. After cooling, the precipitated dye was filtered off, washed with ethyl alcohol and dried. The yield was 0.20 g (45.9%), m.p. 279-280°. After crystallization from ethyl alcohol it consisted of reddish-orange needles with a m.p. of 288-289°.

Found %: N 3.20. $C_{28}H_{21}O_2NS$. Calculated %: N 3.21.

2-(1'-Ethyl-3',3'-dimethylindolinyliden-2'-butenyliden)-indandione-1,3

0.33 g of 2,3,3-trimethylindolenine and 0.32 g of diethyl sulfate were heated in a flask with a reflux condenser on a water bath at 80° for 1 hour. After cooling, the quaternary salt was dissolved by heating in 11.0 ml of n-butyl alcohol and 0.64 g of 2-(acetanilinoallyliden)—indandione-1,3 and 0.25 g of triethylamine were introduced into the solution. The liquid was boiled for 1 hour. After cooling, the dye which was formed was filtered off, washed with ethyl alcohol and dried.

The yield was 0.36 g (48.6%), m.p. 237-238°. After chromatographic purification of a chloroform solution of the dye on active aluminum oxide and crystallization from ethyl alcohol, it consisted of coarse violet prisms with a metallic sheen and a m.p. of 249-250°.

Found %: N 3.91. $C_{25}H_{23}O_2N$. Calculated %: N 3.79.

2-(3'-Ethylbenzthiazolinyliden-2'-butenyliden)-indandione-1,3

0.35 g of the ethyl-p-toluenesulfonate of 2-methylbenzthiazole and 0.32 g of 2-(acetanilinoallyliden)-indandione-1,3 were heated in a flask with a reflux condenser with 13.0 ml of anhydrous ethyl alcohol (incomplete solution). 0.11 g of triethylamine was added to the mixture and the liquid was heated on a boiling water bath for 30 minutes. After cooling, the dye which was formed was filtered off, washed with ethyl alcohol and dried. The yield was 0.20 g (55.5%), and the m.p. 238-240°. After two-fold chromatographic purification of a solution of the dye in chloroform on active aluminum oxide and crystallization from benzene, the dye consisted of green needles with a m.p. of 278-279°.

Found %: N 3.93. $C_{22}H_{17}O_2NS$. Calculated %: N 3.89.

2-(3'-Ethyl-4',5'-diphenylthiazolinyliden-2'-butenyliden)-indandione-1,3

0.62 g of the iodoethylate of 2-methyl-4,5-diphenylthiazole and 0.48 g of 2-(acetanilinoallyliden)-indandione-1,3 were dissolved by heating in 11.0 ml of n-butyl alcohol in a flask with a reflux condenser, and 0.17 g of triethylamine was introduced into the solution. The dark blue liquid was boiled for 30 minutes. A precipitate of the dye was formed shortly after the beginning of the heating. After cooling, the dye was filtered off, washed with ethyl alcohol and dried. The yield was 0.66 g (95.5%), m.p. 258-259°. After chromatographic purification of a chloroform solution of the dye on active aluminum oxide and crystallization from ethyl alcohol, it consisted of fine green prisms with a m.p. of 274-275°.

Found %: N 2.80. $C_{30}H_{23}O_2NS$. Calculated %: N 3.03.

2-(1'-Ethyl-3',3'-dimethylindolinyliden-2'-hexadienyliden)-indandione-1,3

0.65 g of the diethyl sulfate of 2,3,3-trimethylindolenine, obtained by the usual method, was dissolved in 5.0 ml of anhydrous ethyl alcohol in a flask with a reflux condenser by heating; the solution was cooled to 50° and 0.35 g of 2-(acetanilinopentadienyliden)-indandione-1,3 and 0.11 g of triethylamine were added to it. The brownish-yellow mixture was heated at 50° (in a mass) for 5 minutes and left for 24 hours at room temperature. The unreacted 2-(acetanilinopentadienyliden)-indandione-1,3 was then filtered off (weight: 0.22 g), the filtrate was concentrated in a vacuum, the residue dissolved in chloroform, and the solution chromatographed three times on active aluminum oxide; a fraction was collected under these conditions which had a pure blue color. After driving off the chloroform in a vacuum and crystallizing the residue from ethyl alcohol, 0.03 g of the dye was obtained in the form of fine dark brown prisms with a m.p. of 146-147°.

Found %: C 82.10; H 6.40. $C_{27}H_{25}O_2N$. Calculated %: C 81.98; H 6.37.

2-(3'-Ethylbenzthiazolinyliden-2'-hexadienyliden)-indandione-1,3

0.35 g of the ethyl-p-toluenesulfonate of 2-methylbenzthiazole and 0.35 g of 2-(acetanilinopentadienyliden)-indandione-1,3 were dissolved in 10.0 ml of n-butyl alcohol in a flask with a reflux condenser which was heated, and 0.11 g of triethylamine was introduced into the solution; an intense dark blue color at once appeared and the dye precipitated. The mixture was boiled for 15 minutes. After cooling, the precipitate of the dye which was formed was filtered off, carefully washed with cold and hot ethyl alcohol and dried. The yield was 0.15 g (41.7%), m.p. 205-206°. After two-fold crystallization from ethyl alcohol it consisted of fine green prisms with a golden tinge which melted at 207-208°.

Found %: N 3.46. $C_{24}H_{19}O_2NS$. Calculated %: N 3.63.

2-(3'-Ethyl-4',5'-diphenylthiazolinyliden-2'-hexadienyliden)-indandione-1,3

0.41 g of the iodoethylate of 2-methyl-4,5-diphenylthiazole and 0.35 g of 2-(acetanilinopentadienyliden)-indandione-1,3 were dissolved in 10.0 ml of n-butyl alcohol in a flask with a reflux condenser which was heated, and 0.11 g of triethylamine was added to the solution.

The greenish-blue mixture was boiled for 20 minutes. After cooling, the dye which separated was filtered off, washed with ethyl alcohol and dried. The yield was 0.25 g (51.0%), m.p. 184-186°. After chromatographic purification of a chloroform solution of the dye on active aluminum oxide and crystallization from ethyl alcohol, it consisted of fine dark green prisms with a golden tinge, which melted at 200-201°.

Found %: N 2.76. $C_{32}H_{25}O_2NS$. Calculated %: N 2.87.

Triethylamine salt of 2-[3'-Hydroxy-1'-ketoindenyl(1',2')-2-allyliden]-indandione-1,3

0.64 g of 2-(acetanilinoallyliden)-indandione-1,3 and 0.29 g of indandione-1,3 were heated in a flask with

a reflux condenser with 8.0 ml of anhydrous ethyl alcohol (incomplete solution). 0.30 g of triethylamine was added to the mixture; an intense violet color at once appeared. The mixture was heated on a boiling water bath for 40 minutes. After cooling, the alcohol was driven off in a vacuum, the residue (a dark violet oil) was dissolved in chloroform, and the solution was chromatographed on active aluminum oxide; a fraction with a pure violet color was collected under these conditions. After driving off the chloroform in a vacuum and crystallizing the residue from 50% ethyl alcohol, 0.12 g of the triethylamine salt of the dye was obtained in the form of fine, dark brown needles with a m.p. above 300°.

Found %: C 75.46; H 6.32: $C_{27}H_{27}O_4N$. Calculated %: C 75.48; H 6.34.

Triethylamine Salt of 2-[3'-Hydroxy-1'-ketoindenyl(1',2')-2''-pentadienyliden]-indandione-1,3

1.46 g of indandione-1,3 and 1.42 g of the hydrochloride of the dianil of glutaconic aldehyde were dissolved in 20.0 ml of anhydrous ethyl alcohol in a flask with a reflux condenser which was heated, and 1.50 g of triethylamine was introduced into the solution. The dark blue liquid was heated on a boiling water bath for 30 minutes. After cooling, the precipitate of 2-(anilinopentadienyliden)-indandione-1,3 formed was filtered off and washed with 3.0 ml of anhydrous ethyl alcohol (the weight of the precipitate was 0.80 g, the m.p. 232-236° and a mixed sample with the pure substance displayed no melting point depression). The filtrate was combined with the wash alcohol and concentrated in a vacuum to a volume of 3.0 ml; an abundant precipitate of the triethylamine salt of the dye thereupon settled out and was filtered off, washed with alcohol and dried in a vacuum over caustic alkali. The yield was 0.20 g (8.7%), the m.p., 148-150°. After crystallization from ethyl alcohol it consisted of dark green prisms with a m.p. of 149-150°.

Found %: C 76.51; H 6.45
$C_{29}H_{29}O_4N$. Calculated %: C 76.44; H 6.42

The absorption spectra of the dyes were measured in a $1 \cdot 10^{-4}$ molar solution with a König-Martens spectrophotometer and in a few cases, with a "UM-2" monochomator.

SUMMARY

1. The synthesis of several di-, tetra- and hexamethinmerocyanines which are derivatives of indandione-1,3, and also of the corresponding tri- and pentamethinoxanines was carried out. The absorption spectra of these merocyanines was investigated in mixtures of solvents which were close in their properties but had varying polarity.

2. It was shown that the majority of the merocyanines which are derivatives of indandione-1,3 are characterized by a comparatively regular distribution of the electron density in the polymethine chromophore and by reduced polarizability.

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INVESTIGATION OF FURAN COMPOUNDS

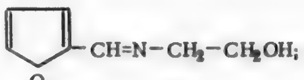
VI. FURAN AND TETRAHYDROFURAN AMINO ALCOHOLS FROM FURFURAL AND β-(α-FURYL)-ACROLEIN

A. A. Ponomarev, V. Pletneva, V. Sedavkina and L. Barskaya

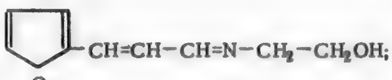
The condensation of furfural with primary aliphatic amines, as is well-known, leads to the formation of the corresponding azomethines.

Very little is known of the reaction of furfural and its vinyl analogs with amino alcohols. In particular, Senkus [1] described a product, prepared from furfural and β-aminoisobutanol, which, in the opinion of the author, was the oxazolidine derivative; upon hydrogenation of the latter, the corresponding furfurylaminoalkanol was formed.

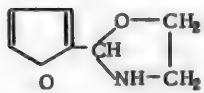
As our experiments have shown, furfural and β-(α-furyl)-acrolein react with monoethanol amine in a mole-for-mole ratio without catalyst, to form the corresponding derivatives in excellent yields. The latter can have the structure of azomethines (I and II) or of their isomeric oxazolidine compounds (III and IV), the formation of which is possible as a result of intramolecular cyclization:



(I)



(II)



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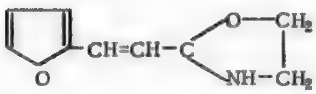
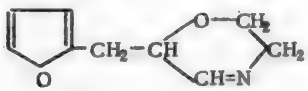


(IV)

In the case of furylacrolein, a third formula with a morpholine ring is also possible:



(V)

The sensitivity of these substances to acidic reagents, oxidizing agents etc., complicates the elucidation of their structure by the usual chemical methods. This applies also to the derivatives of other aldehydes and mono-alkanol amines; this can be explained by the fact that the oxazolidine structure ascribed to many of them is, properly speaking, unfounded [2, 3, 4]. In this connection it should be indicated that the study of the infra-red spectra of a number of analogous derivatives of aromatic aldehydes and monoethanol amines gives us a basis for assuming that their structure is azomethinic, but not cyclic (oxazolidinic) [5].

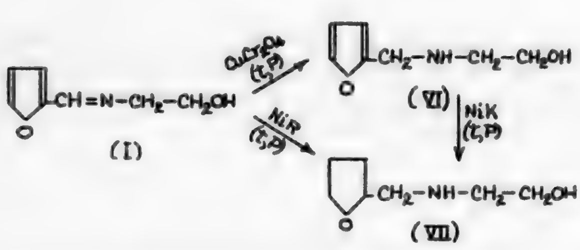
The molecular refraction of the substances obtained by us makes it clear that they have the azomethine structures (I) and (II). Actually, the experimentally found molecular refraction of the first product is 38.82, while that calculated for formula (I) is equal to 37.24 (EMR_D 1.58), and for III, 36.08 (EMR_D 2.74). While the presence of an excited state is a consequence of the structure of the azomethine (the presence of a conjugated exocyclic double bond in the ring), such a considerably excited state can not be explained for the oxazolidine derivative (III) by any structural peculiarities.

In the same way, the observed value of MR_D for the second product amounted to 51.79; that calculated for formula (II) (azomethine), 46.00 (EMR_D 5.78), and for formula (IV), 44.39 (EMR_D 7.40), and for formula (V), 44.85 (EMR_D 6.94). It is evident that in this case, if the structure of the substance was in accord with formula (IV) on (V), the observed experimental MR_D would have had to have been considerably less than occurs, in accord with the considerations already stated in connection with the first product.

In this connection it is impossible not to note that the experimental EMR_D found by us for the products (I) and (II) is in accord in absolute magnitude with the EMR_D of other furan derivatives which have, respectively, one or two double bonds in conjugation with the ring. Thus, for example, the EMR_D of furfural is 1.61, of furylethylene, 1.63 [6], etc.; the EMR_D of furylacrolein is 5.70 [7], of β-(5-methyl-2-furyl)-acrolein is 5.62 [8], of furylbutenone 5.52 [6], etc..

This agreement in the magnitudes of the EMR_D is also a well-known confirmation of the azomethinic nature of the indicated products. In addition, it is evidence of the fact that the double bonds of the $>C=C<$, $>C=O$ and $>C=N-$ type in conjugation with carbon-carbon double bonds of the furan ring exert an almost identical exciting influence.

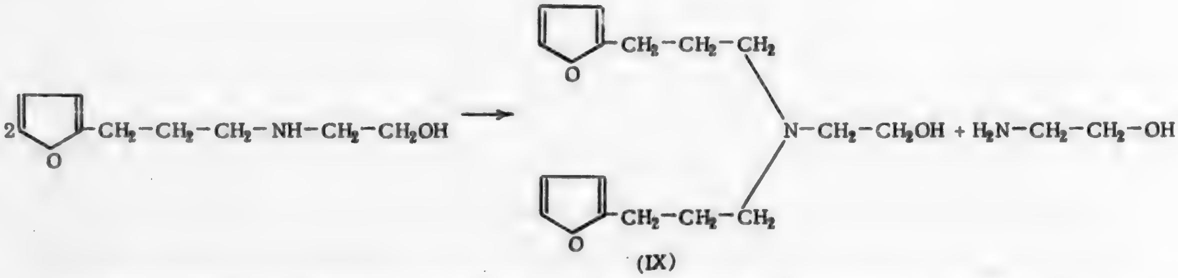
The experiments involving the hydrogenation of the azomethines were performed in the presence of various catalysts. It was established that the end products of the hydrogenation of furfurylidenaminoethanol (I), depending on the catalyst and the conditions, are either furfurylamino ethanol (VI) or tetrahydrofurfurylaminoethanol (VII), which is illustrated by the following scheme:



The best yield of (VI) (70-72%) was obtained with the use of $CuCr_2O_4$ while the best yield of (VII) was obtained by the hydrogenation of (VI) with nickel on kieselguhr (NiK) (73%).

(α-Furylpropyl)-amino ethanol (VIII) was obtained in a yield of 41.5% by the hydrogenation of (II) with Raney nickel (NiR) at 140-160° and a pressure of 100 atm.

When (II) was hydrogenated under other conditions, with the same catalyst (170°, 125 atm), (α-furylpropyl)-amino ethanol (VIII), bis-(α-furylpropyl)-aminoethanol (IX) and monoethanolamine were isolated from the reaction mixture. It can, consequently, be assumed that the process proceeds initially to the formation of (VIII) and then is complicated by a disproportionation reaction of (VIII) into (IX) and monoethanolamine:



The corresponding N-aceto derivatives were obtained by the action of acetic anhydride on furfurylaminoethanol, tetrahydrofurfurylaminoethanol and (α-furylpropyl)-aminoethanol:

$$R-NH-CH_2-CH_2OH \xrightarrow{(CH_3CO)_2O} R-\underset{\substack{|\\ COCH_3}}{N}-CH_2-CH_2OCOCH_3$$

Attempts to obtain an azomethine in the pure form from furfurylidenacetone and monoethanolamine were not successful in view of the considerable resinification (particularly on distillation) of the reaction products.

EXPERIMENTAL

The hydrogenation was conducted in steel rotating autoclaves, 0.5 and 0.15 liter in capacity. The temperature was held within the assigned limits by an electronic regulating millivoltmeter. The preparation of the catalysts was as follows: Raney nickel (NiR) was prepared by leaching Ni—Al alloy [9]; copper chromite catalyst ($CuCr_2O_4$) was prepared by the usual method [10]; platinum catalyst was prepared by Adam's method [11]. The nickel on kieselguhr (NiK) was industrial catalyst of Soviet production, which was preliminarily ground and reduced in a stream of hydrogen at 200°.

N-Furfurylidenaminoethanol

In a typical experiment, 27 g of furfural was placed in a three-necked flask, 0.5 liter in capacity, equipped with a mechanical stirrer with an oil seal and a dropping funnel, and then 17.7 g of monoethanolamine was added from the dropping funnel to the flask while the contents of the latter were being stirred over a period of 2 hours. The color of the reaction mixture changed during the experiment from straw-yellow to cherry-brown and the mixture thickened. After the addition of all the monoethanolamine, the contents of the flask were heated for half an hour on a water bath at 60-70° and then were vacuum distilled in a stream of nitrogen. The furfurylidenaminoethanol distilled at 136° (8 mm) and the weight was 27.5 g (70.3%).

d_4^{20} 1.1524; n_D^{20} 1.5561; MR_D 38.82; calculated 37.24.

0.1342 g sub.: 0.2954 g CO_2; 0.0830 g H_2O. 0.1737 g sub.: 15.6 ml N_2 (23.4°, 748 mm). 0.1778 g sub.: 16 ml N_2 (25°, 768 mm). 0.0726 g sub.: 13.6 ml CH_4 (22°, 767 mm). Found %: C 60.07; H 6.92; N 10.34, 10.19; active H 0.76. $C_7H_9O_2N$. Calculated %: C 60.42; H 6.52; N 10.07; active H 0.72.

By conducting the reaction in a nitrogen atmosphere and subsequent vacuum distillation of the product in a stream of nitrogen, the yield was raised to 82%; the reaction product, when not distilled in a stream of nitrogen, has a darker color and a lower index of refraction. However, pure azomethine, which has the above indicated constants, is obtained by repeated vacuum distillation even in this case.

Furfurylidenaminoethanol consisted of a straw-yellow liquid which quickly thickened and darkened in air, and had the characteristic amine odor. It was quite soluble in water, alcohol and ether. The b.p. was 114° (1.5 mm), 123-124° (4 mm).

Furfurylaminoethanol

110 g of freshly distilled furfurylidenaminoethanol, 140 ml of dioxan and 7 g of copper-chromite catalyst was placed in an 0.5 liter rotating autoclave. The initial hydrogen pressure was 70 atm, and the temperature 110-115°. The hydrogenation was completed after the absorption of approximately 23 liters of hydrogen (1.2 mole per mole of substance). After elimination of the catalyst by filtration, the dioxan was driven off under reduced pressure and the residue was vacuum distilled.

A fraction was obtained with a b.p. of 115-116° (3 mm), 87.3 g (71%) in weight.

d_4^{20} 1.1184; n_D^{20} 1.5032; MR_D 37.32; calculated 38.16.

0.1285 g sub.: 11.6 ml N_2 (22°, 741 mm). 0.1301 g sub.: 12 ml N_2 (21°, 747 mm). Found %: N 9.98, 10.2. $C_7H_{11}O_2N$. Calculated %: N 9.92.

* The molecular weight was determined in dioxan, since exaggerated results were obtained with the determination in benzene.

0.1873 g sub.: 16.03 g dioxan: Δt 0.38°. Found: M 145.2. $C_7H_{11}O_2N$. Calculated: M 141.16.

Furfurylaminoethanol with a b.p. of 113-116° (3 mm) was obtained in a yield of 43% by hydrogenation of furfurylidenaminoethanol in alcoholic solution with a platinum catalyst at atmospheric pressure and room temperature.

d_4^{20} 1.1120; n_D^{20} 1.5028; MR_D 37.51.

0.1442 g sub.: 13.2 ml N_2 (23°, 755 mm). 0.1993 g sub.: 18.2 ml N_2 (24°, 754.9 mm). 0.0197 g sub.: 7.2 ml CH_4 (22°, 760.8 mm). Found %: N 10.37, 10.26; active H 1.47. $C_7H_{11}O_2N$. Calculated %: N 9.92; active H 1.42.

Furfurylaminoethanol was also obtained by hydrogenation of furfurylidenaminoethanol in an autoclave in dioxan solution in the presence of nickel on kieselguhr (10% in relation to the weight of the substance); the initial hydrogen pressure was 105 atm, the temperature 120-130°. A product with a b.p. of 123° (6 mm); d_4^{20} 1.1110; n_D^{20} 1.5021; MR_D 37.50. The yield was 50%.

Furfurylaminoethanol was a mobile, light yellow liquid with a weak amine odor and a sharp taste, which somewhat darkened during prolonged storage. It was quite soluble in water, alcohol, ether and acetic anhydride. It had an anesthetic action.

N-Acetofurfurylaminoethanol Acetate

8 g of furfurylaminoethanol and 30 g of acetic anhydride were placed in an assay autoclave, 50 ml in capacity; the autoclave was heated in a shaking tubular furnace for 1 hour to 200-220°. After the autoclave had cooled, the reaction mixture was extracted, the acetic anhydride and acetic acid driven off, and the residue vacuum distilled. 12 g (94%) of a light yellow liquid with a b.p. of 157° (2.5 mm) was obtained.

d_4^{20} 1.1614; n_D^{20} 1.4897; MR_D 56.04; claculated 56.98.

0.1463 g sub.: 8.4 ml N_2 (26°, 759.5 mm). 0.1531 g sub.: 8.6 ml N_2 (22°, 741 mm). Found %: N 6.42, 6.21. $C_{11}H_{15}O_4N$. Calculated %: N 6.22.

There were no active hydrogen atoms present in the substance (as determined by Terentyev's method).

Acetofurfurylaminoethanol acetate is soluble in alcohol, acetic anhydride, benzene and dioxan.

Tetrahydrofurfurylaminoethanol

50.5 g of furfurylaminoethanol, 90 ml of dioxane and 4 g of NiK were placed in a rotating autoclave, 0.5 liter in capacity and hydrogenated at an initial hydrogen pressure of 94 atm and a temperature of 120-140°. The hydrogenation was concluded at an absorption of approximately 13.5 liters of H_2, which was equivalent to 1.55 mole per 1 mole of the substance.

By vacuum distilling the residue after elimination of the catalyst and solvent, 36.9 g of a basic fraction with a b.p. of 142-143° (23 mm) was obtained. The yield was 73.1%.

d_4^{20} 1.0780; n_D^{20} 1.4821; MR_D 38.42; calculated 39.09.

0.1301 g sub.: 11 ml N_2 (21°, 764 mm). 0.1179 g sub.: 9.9 ml N_2 (22°, 747 mm). 0.0180 g sub.: 5.8 ml CH_4 (24°, 758 mm). Found %: N 9.68, 9.62; active H 1.27. $C_7H_{15}O_2N$. Calculated %: N 9.64; active H 1.38. 0.2005 g sub.: 17.53 g dioxan; Δt 0.36°. Found: M 149.6. $C_7H_{15}O_2N$. Calculated: M 145.19.

When 38 g of furfurylidenaminoethanol in anhydrous alcohol was hydrogenated with NiR at 150-160° and an initial hydrogen pressure of 120 atm, the hydrogenation was completed with the absorption of approximately 2.4 moles of H_2 per 1 mole of the substance. As a result of the 2-fold fractionation of the catalyzate in a vacuum, 18.54 g (48%) of tetrahydrofurfurylaminoethanol with a b.p. of 123-124° (4 mm) was obtained; there was a considerable quantity of resin in the residue.

d_4^{20} 1.0676; n_D^{20} 1.4812; MR_D 38.72; calculated 39.09.

0.1182 g sub.: 0.2518 g CO_2; 0.1086 g H_2O. 0.1547 g sub.: 14 ml N_2 (25°, 757.5 mm). 0.1580 g sub.: 14 ml N_2 (24°, 755 mm). 0.0136 g sub.: 4.4 ml CH_4 (21°, 756.8 mm). Found %: C 58.11; H 10.28; N 10.09, 10.14; active H 1.30. $C_7H_{15}O_2N$. Calculated %: C 57.92; H 10.41; N 9.64; active H 1.38.

Tetrahydrofurfurylaminoethanol is a colorless liquid with a sharp taste, stable when stored. It is quite soluble in water, alcohol, benzene, dioxan, acetic anhydride and acetic acid; the pH of an aqueous solution is 9.0 (determined with a set of indicator papers).

Tetrahydrofurfurylaminoethanol forms characteristic precipitates with aqueous solutions of the salts of the divalent metals — for example, the precipitate with Cu^{++} ions is light brown, with Mn^{++} is light violet, etc..

N-Acetotetrahydrofurfurylaminoethanol Acetate

The acetylation was conducted in two assay autoclaves, 50 ml in capacity, into each of which 8 g of tetrahydrofurfurylaminoethanol, 30 g of acetic anhydride and 0.5 g of roasted $ZnCl_2$ were introduced. The autoclaves were heated in a shaking tubular furnace for 1.5 hours at 170°. After eliminating the acetic anhydride and acetic acid, the residue was vacuum distilled, and 15.7 g of a yellowish liquid with a b.p. of 153° (2.5 mm); d_4^{20} 1.136; n_D^{20} 1.4780 was thereby obtained.

The substance was again vacuum distilled at 1.5 mm for analysis and had a b.p. of 149.5-150°.

d_4^{20} 1.1379; n_D^{20} 1.4792; MR_D 57.16; calculated 57.91.

0.1292 g sub.: 7.4 ml N_2 (24°, 744 mm). 0.1528 g sub.: 8.5 ml N_2 (27°, 751 mm). Found %: N 6.37; 6.21. $C_{11}H_{19}O_4N$. Calculated %: N 6.11.

0.1140 g sub.: 19.82 g benzene: Δt 0.14°. Found: M 211.2. $C_{11}H_{19}O_4N$. Calculated: M 229.26.

There were no active hydrogen atoms in the substance (Terentyev determination).

N-Acetotetrahydrofurfurylaminoethanol acetate is soluble in alcohol, dioxan, benzene, acetic anhydride and acetic acid.

Azomethine from Furylacrolein and Monoethanolamine

36.6 g of freshly distilled furylacrolein was dissolved in 30 ml of anhydrous alcohol, placed in a three-necked flask which was equipped with a mechanical stirrer and a separatory funnel, and 18.4 g of ethanolamine was added over a period of 2 hours while the mixture was carefully stirred. Under these conditions, a change in color and a small evolution of heat in the mixture were observed. The mixture was then stirred for 30 minutes more, while being heated on a water bath to 50°. The alcohol was distilled off under reduced pressure. 43 g of a fraction which boiled at 153-156° (3 mm) was removed by vacuum distillation; the yield was 86.8%. The yield of product reached 91% in other experiments. It consisted of a viscous, yellow colored liquid which rapidly darkened in air.

d_4^{20} 1.1194; n_D^{20} 1.6190; MR_D 51.79; calculated 46.00.

0.2795 g sub.: 17.2 ml 0.1 N H_2SO_4. 0.2183 g sub.: 13.5 ml 0.1 N H_2SO_4. Found %: N 8.61, 8.66. $C_9H_{11}O_2N$. Calculated %: N 8.48.

(α-Furylpropyl)-aminoethanol

43 g of freshly distilled azomethine was dissolved in 100 ml of anhydrous alcohol and hydrogenated in an 0.5 liter rotating autoclave in the presence of 4 g of Raney nickel at an initial hydrogen pressure of 109 atm and a temperature of 140-160°. The drop in pressure was equivalent to an absorption of approximately 2 moles of hydrogen per 1 mole of substance.

After elimination of the solvent and catalyst, the catalyzate was subjected to fractional distillation in a vacuum, as a result of which 18.3 g (41.5%) of a fraction with a b.p. of 134-135° (4.5 mm) was obtained.

d_4^{20} 1,0608; n_D^{20} 1.4970; MR_D 46.65; calculated 47.40.

0.2948 g sub.: 22 ml N_2 (21°, 755 mm). 0.3040 g sub.: 23.65 ml N_2 (25°, 764 mm). Found %: N 8.45, 8.75. $C_9H_{15}O_2N$. Calculated %: N 8.28. 0.1966 g sub.: 16.75 g dioxan: Δt 0.31°. Found: M 178.3. $C_9H_{15}O_2N$. Calculated: M 169.22.

The Verley method was used for the joint determination of the percentage content of the (NH + OH) groups.

0.3010 g sub.: 8.65 ml 0.5 N KOH (K = 0.8316). 0.2523 g sub.: 7.45 ml 0.5 N KOH (K = 0.8316). Found %: (OH + NH) 19.11, 19.64. $C_9H_{13}O$ (NH + OH). Calculated %: (OH + NH) 18.91.

N-Aceto-(α-furylpropyl)-aminoethanol Acetate

The acetylation was carried out in an assay autoclave at a temperature of 200° for 3 hours. 7.5 g of the amino alcohol, 1 g of roasted $ZnCl_2$ and 24 g of acetic anhydride were taken. The excess of acetic anhydride and acetic acid was distilled off; it was detected that about 8 g (2 equivalents) of acetic anhydride reacted. The residue was vacuum distilled and 7.6 g of a fraction with a b.p. of 152-165° (1 mm) was collected. As a result of a repeated distillation, 5.7 g of a thick liquid, which fluoresced in the freshly distilled state and had a b.p. of 165-168° (1 mm), was removed.

d_4^{20} 1.1196; n_D^{20} 1.4872; MR_D 65.09; calculated 66.22.

0.1109 g sub.: 0.0735 g H_2O; 0.2480 g CO_2. 0.1505 g sub.: 0.1024 g H_2O; 0.3392 g CO_2. 0.2108 g sub.: 11.6 ml N_2 (26°, 761 mm). 0.2459 g sub.: 13 ml N_2 (25°, 743 mm). Found %: C 61.23, 61.51; H 7.42, 7.55; N 6.15, 5.78. $C_{13}H_{19}O_4N$. Calculated %: C 61.52; H 7.56; N 5.53. 0.1470 g sub.: 17.73 g benzene: Δt 0.17°. 0.1612 g sub.: 18.24 g benzene: Δt 0.18°. Found: M 250.8, 252.4. $C_{13}H_{19}O_4N$. Calculated: M 253.3

In another experiment involving the hydrogenation of azomethine, which was carried out at an initial hydrogen pressure of 125 atm and 170°, 55 g of substance, 180 ml of dioxane and 7 g of NiR (12% in relation to the substance being hydrogenated) were taken. The hydrogen absorption calculated on the weight of the

hydrogenated product was approximately equivalent to that required for the reduction of two double bonds. After eliminating the catalyst and distilling off the solvent, the residue was vacuum distilled at 1.5 mm. The following basic fractions were obtained: 1st fraction with a b.p. of 55-56°, n_D^{20} 1.4585, 2.2 g; 2nd fraction, b.p. 114-116°, n_D^{20} 1.4960, 9.65 g; and 3rd fraction, b.p. 172-174°, n_D^{20} 1.5492, 15.4 g.

The 1st fraction was again distilled at atmospheric pressure and boiled within the limits 164-168°; n_D^{20} 1.4570. The hydrochloride with a m.p. of 98-100° was obtained by passing dry HCl into a solution of the substance in anhydrous ether; it consisted of white crystals which deliquesced in air. On the basis of these data, it can be considered established that the substance was monoethanolamine (literature data: b.p. 169-171°, n_D^{20} 1.4539, hydrochloride – white crystals, m.p. 100°).

The 2nd fraction, as follows from its physical properties, was the previously described (α-furylpropyl)-aminoethanol.

d_4^{20} 1.06; n_D^{20} 1.4960; MR_D 46.6.

The 3rd fraction, as can be assumed on the basis of the data which follow below, was bis-(α-furylpropyl)-aminoethanol.

d_4^{20} 1.1370; n_D^{20} 1.5492; MR_D 77.61; calculated 78.57.

0.1542 g sub.: 0.1060 g H_2O; 0.3932 g CO_2. 0.1647 g sub.: 0.1123 g H_2O; 0.4198 g CO_2. 0.3192 g sub.: 16.2 ml N_2 (20°, 759 mm). 0.2854 g sub.: 13.9 ml N_2 (22°, 762 mm). 0.1484 g sub.: 12.8 ml CH_4 (24°, 762 mm). 0.1454 g sub.: 14.6 ml CH_4 (22°, 758 mm). Found %: C 69.59, 69.56; H 7.69, 7.63; N 5.8, 5.53; active H 0.34, 0.39. $C_{16}H_{23}O_3N$. Calculated %: C 69.3; H 8.29; N 5.05; active H 0.36. 0.3013 g sub.: 10.55 g benzene: Δt 0.534°. 0.3385 g sub.: 14.89 g benzene: Δt 0.425°. Found: M 274.9, 274.9. $C_{16}H_{23}O_3N$. Calculated: M 277.3.

The product was a very viscous liquid with a yellow color; was soluble in alcohol, ether, benzene, dioxan and in xylene on heating, and was insoluble in water.

SUMMARY

1. It was shown that furfural and β-(α-furyl)-acrolein react with monoethanolamine without catalyst, with the formation of the corresponding azomethines in excellent yields.

2. Experiments were described involving the hydrogenation under various conditions of the azomethines indicated above, as a result of which the following were obtained: furfurylaminoethanol, tetrahydrofurfurylaminoethanol, (α-furylpropyl)-aminoethanol and bis-(α-furylpropyl)-aminoethanol.

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* See Consultants Bureau Translation, page 1811.

REACTION OF CERTAIN ALCOHOLS WITH 2-NITROINDANDIONE-1,3

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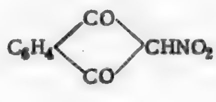
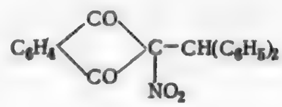
Several years ago, one of us with his coworkers showed [1] that 2-nitroindandione-1,3 (I) condenses very readily with benzhydrol to form 2-nitro-2-benzhydrylindandion-1,3 (II). Cleavage of the five-membered ring readily proceeds as a result of the action of aqueous or alcoholic alkali, and the unstable acid (III) is formed, which readily closes the ring again with formation of an isomeric product, the structure of which is still not entirely clear.



(I)



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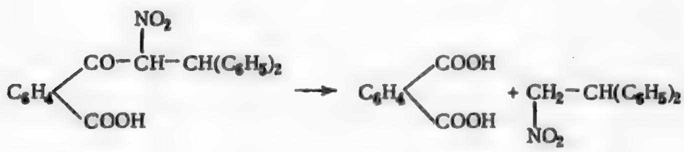


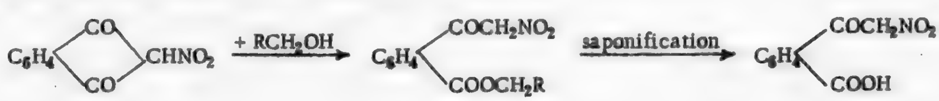
(III) (IV)

The more energetic action of alkali or alcoholate cleaves the phthalic acid with formation of benzhydrylnitromethane or β,β-diphenyl-α-nitroethane (IV). Thus, with the aid of nitroindandione, the nitromethyl group was successfully substituted for the hydroxyl group of benzhydrol as the end result of a series of readily-proceeding reactions

$$(C_6H_5)_2CHOH \rightarrow (C_6H_5)_2CHCH_2NO_2.$$

In order to determine to what extent this "nitromethylation" reaction with the aid of nitroindandione is general, the investigation was extended to other hydrols and often gave positive results.

L. Zalukaev investigated, simultaneously with these works, the reaction of methyl and ethyl alcohols with nitroindandione and found [2] that the reaction proceeds differently with these alcohols. These alcohols, analogously to alkalis or alcoholates, cleave the five-membered ring of nitroindandione with the formation of the esters of ω-nitroacetophenone-o-carboxylic acid (V). These esters are readily saponified and yield the free acid (VI), which has already been described in the literature:

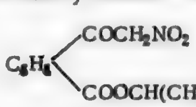


(V) (VI)

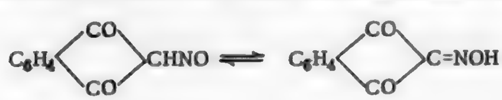
R = H or CH_3

It was of interest to investigate how other alcohols, above all, secondary aliphatic alcohols, would behave: would they react similarly to benzhydrol or similarly to methyl and ethyl alcohols?

Experiments set up with isopropyl alcohol showed that the course of the reaction depends on the conditions under which it is carried out. If a comparatively great excess of isopropyl alcohol is taken, then the reaction proceeds analogously to methyl and ethyl alcohols, and the isopropyl ester of ω-nitroacetophenone-o-carboxylic acid (VII) is chiefly formed. The free acid (VI) which has already been mentioned is formed by its saponification:



(VII)



(VIII)

The yields of the ester in general did not exceed 33% of the theoretical. Attempts to use ether, acetone, water, benzene and xylene as the solvent did not give positive results. When ethyl alcohol was used as the solvent, the ethyl ester of ω-nitroacetophenone-o-carboxylic acid (V,R = CH_3) was formed. However, the cleavage of the five-membered ring of nitroindandione and formation of the isopropyl ester of ω-nitroacetophenone-o-carboxylic acid proceeds in glacial acetic acid solution even when quite little isopropyl alcohol is taken. The ready cleavage of the indandione ring is a rather unusual phenomenon (in contrast to the cleavage of this ring in acidic medium by alcohol,which is a phenomenon generally known and described in the literature). Some results are given in the table.

TABLE

Expt. No.	Nitro-indan-dione (g)	Isopropyl alcohol (ml)	Glacial acetic acid (ml)	Duration of the heating (mins.)	Yield of isopropyl ω-nitroacetophenone-o-carboxylate (g)	in % of the nitroindandione
1	2.30	22	–	10	0.20	–
2	2.30	22	–	20	0.40	–
3	2.30	22	–	30	0.60	–
4	2.30	22	–	40	0.65	–
5	2.30	33	–	40	0.70	27.0
6	2.30	22	–	60	0.70	27.0
7	2.30	33	–	60	0.80	33.3
8	1.15	1.1	10	15	0.30	Together with resinous substances
9	1.15	2.2	5	15	0.30	
10	1.15	2.2	10	10	0.20	

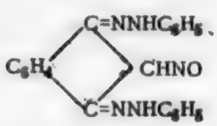
If considerably less isopropyl alcohol is taken (for example 20 ml of alcohol per 10 g of nitroindandione), the the reaction proceeds differently. The liquid becomes dark red colored and acetone is evolved. 2-Nitroso-indandione-1,3 (VIII) was isolated from the reaction products. It is evident that the nitroindandione here acts as an oxidizing agent which oxidizes the isopropyl alcohol to acetone, and is itself reduced to nitrosoindandione. A similar reaction was noted in due course with formic acid [3].

Careful investigation showed that nitrosoindandione is also formed by the reaction of nitroindandione with methy, ethyl, isobutyl and other alcohols. In the case of the primary alcohols, however, the yields of nitrosoindandione are very small. They are also small with cyclohexanol. Excellent yields of nitrosoindandione are obtained with benzyl alcohol (72.9%); with acenaphthenol, nitrosoindandione was obtained in a yield of 82.9%.

The properties of nitrosoindandione have been very scantily described in the literature [3, 4]; it was thus not easy to recognize it at once and the nitrosoindandione obtained was, consequently, studied in somewhat greater detail.

It is insoluble in ether and cold water; difficultly soluble in chloroform; more soluble in hot water, hot alcohol, glacial acetic acid. It dissolves with a yellow color in pyridine and upon addition of water the following sequence of color changes is observed: yellow, green, green-violet, red-violet. It dissolves with a red-violet color in solutions of alkali and ammonia and also of sodium carbonate. It gives the indophenine reaction with benzene which contains thiophene and concentrated sulfuric acid; this can be explained by the fact that the nitrosoindandione is partially converted into indantrione oxime which is cleaved to indantrione, and the latter, as experiments have shown, actually gives the indophenine reaction. It is characteristic, however, that nitrosoindandione itself can not be cleaved [5] to indantrione (ninhydrin), which is evidence in favor of the nitroso form [3]. On heating with 10% sodium hydroxide, phthalic acid and sodium cyanide are formed.

2,2-Dibromindandione-1,3 is formed by the action of bromine on nitrosoindandione. The bis-phenylhydrazone (IX) is formed with phenylhydrazine:



(IX)

It has already been noted in due course [3], that the melting point of nitrosoindandione depends on the speed of heating the substance. It proved also to be dependent on the solvent from which the nitrosoindandione was recrystallized. Thus, for example, on heating nitrosoindandione under as identical conditions as possible, it melted at 216-218° when recrystallized from glacial acetic acid, at 204-206° when crystallized from water, at 215-216° after a secondary crystallization from glacial acetic acid, and at 201-202° after a secondary crystallization from water. It is possible that both tautomeric forms (VIII), are formed here. The question was not investigated in greater detail.

EXPERIMENTAL

Isopropyl ω-Nitroacetophenone-o-carboxylate (VII)

2.3 g of nitroindandione and 33 ml of isopropyl alcohol were heated on a water bath for approximately 1 hour. The nitroindandione gradually dissolved and the liquid began to assume a dark red color. When the reaction was terminated at this moment, the best yields were obtained. After cooling, the solution, it was diluted with a 5-10 fold quantity of water. Needle-like crystals then precipitated together with a small amount of an oily substance, which was readily soluble in ether and thus readily separable. This oily product was dissolved in concentrated sulfuric acid with a green fluorescence. After the ether treatment, the residue was recrystallized from acetic acid (1:1) and 0.8 g of isopropyl ω-nitroacetophenone-o-carboxylate was obtained, which amounted to 33.3% of the theoretical. The m.p. was 70-71°.

4.114 mg sub.: 0.222 ml N_2 (20°, 764 mm). Found %: N 6.01. $C_{12}H_{11}O_4N$. Calculated %: N 6.32.

When the isopropyl ω-nitroacetophenone-o-carboxylate was dissolved in 2.0 N sodium hydroxide, saponification of the ester occurred. The free ω-nitroacetophenone-o-carboxylic acid was isolated by acidifying the solution. The m.p. was 122-123°, which was in accord with the literature data (121.5°).

3.400 mg sub.: 0.194 ml N_2 (21°, 754 mm). Found %: N 6.57. $C_9H_7O_5N$. Calculated %: N 6.72.

Isobutyl (Primary) ω-Nitroacetophenone-o-carboyxlate (V, R=$CH(CH_3)_2$)

It was obtained analogously to the preceding. The m.p. was 89-90°.

4.200 mg sub.: 0.198 ml N_2(20°, 749 mm). Found %: N 5.42. $C_{13}H_{13}O_4N$. Calculated %: N 5.67.

Reduction of Nitroindandione with Isopropyl Alcohol

10 g of nitroindandione and 20 ml of isopropyl alcohol were heated on a water bath for 2 hours. The solution became dark red in color and acetone was evolved: a paper, moistened with o-nitrobenzaldehyde and alkali, became blue colored when held in the vapors with the formation of indigo. The reaction liquid was diluted with an approximately 5-fold quantity of water. A yellow crystalline precipitate settled out together with an oily substance. After treatment with ether and crystallization from glacial acetic acid, 2 g of the nitrosoindandione (VIII) was obtained which amounted to 28.6% of the theoretical. The m.p. was 217-218°.

3.886, 3.271 mg sub.: 0.270 ml N_2 (22°, 752 mm), 0.225 ml N_2 (18°, 758 mm). Found %: N 8.14, 8.05. $C_9H_5O_3N$. Calculated %: N 8.00.

Reduction of Nitroindandione with Benzyl Alcohol

12 g of nitroindandione and 24 ml of benzyl alcohol were heated on a water bath. In about 20 minutes the nitroindandione dissolved and the solution assumed a dark red color. In the course of 30 minutes, a vigorous reaction occurred and yellow crystals appeared. The yield of 6.8 g of nitrosoindandione (VIII) amounted to 68.3% of the theoretical. The reddish-brown filtrate was shaken with 10% sodium carbonate solution, the aqueous layer was separated and acidified. Needle-like green crystals of nitrosoindandione precipitated. After crystallization from glacial acetic acid, the m.p. was 216-217° and after crystallization from water, it was 208-212°. The total yield of nitrosoindandione was 7.3 g (72.9%).

2.386 mg sub.: 0.162 ml N_2 (19°, 747 mm). Found %: N 7.80. $C_9H_5O_3N$. Calculated %: N 8.00.

Benzaldehyde was contained in the reddish-brown filtrate; this was shown both by qualitative reactions for aldehydes and by formation of the semicarbazone. The m.p. was 225-228° (222, 227° according to the literature data).

2.743 mg sub.: 0.613 ml N_2 (21°, 764 mm). Found %: N 26.08. $C_8H_9ON_3$. Calculated %: N 25.76.

Reduction of Nitroindandione with Acenaphthenol

2.3 g of nitroindandione, 2.6 g of acenaphthenol and 15 ml of glacial acetic acid were heated to boiling for 5-10 minutes. A vigorous reaction occurred and a yellow precipitate of nitrosoindandione was formed. The yield of 1.6 g amounted to 82.9% of the theoretical. It was not different in its properties from the nitrosoindandione described above.

2.886 mg sub.: 0.200 ml N_2 (22°, 760 mm). Found %: N 8.02. $C_9H_5O_3N$. Calculated %: N 8.00.

2,2-Dibromindandione from Nitrosoindandione

1.5 g of nitrosoindandione was drenched with excess bromine water. The yellow nitrosoindandione was converted into the white 2,2-dibromindandione-1,3 which was insoluble in water. After crystallization from glacial acetic acid, the m.p. was 178°, which was in accord with the literature data. A mixture with known 2,2-dibromindandione displayed no melting point depression.

Bis-phenylhydrazone of Nitrosoindandione (IX)

2 g of nitrosoindandione in aqueous solution was heated with an aqueous solution of 5 g of phenylhydrazine hydrochloride. A flocculent, dark red precipitate was quickly formed. After crystallization from dilute ethyl alcohol, orange needles of the bis-phenylhydrazone with a m.p. of 201° were obtained.

3.729 mg sub.: 0.637 ml N_2 (18°, 758 mm). 4.057 mg sub.: 0.696 ml N_2 (19°, 759 mm). Found %: N 19.99, 20.03. $C_{21}H_{17}ON_5$. Calculated %: N 19.71.

SUMMARY

On heating nitroindandione with a large excess of isopropyl or primary isobutyl alcohol, cleavage of the five-membered ring of nitroindandione occurs and the corresponding ester of ω-nitroacetophenone-o-carboxylic acid is formed.

On heating nitroindandione with a small excess of isopropyl or benzyl alcohol, and also with acenaphthenol, oxidation of these alcohols into the corresponding aldehyde or ketone occurs, while the nitroindandione is reduced to nitrosoindandione. The properties of this last compound were studied in greater detail.

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* See Consultants Bureau Translation, page 1543.

INVESTIGATION OF THE PRODUCTS OF THE CONDENSATION OF N-METHYLTRYPTAMINE WITH FORMALDEHYDE

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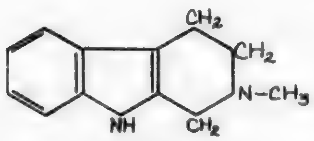
With the object of investigating the mechanism of the reciprocal reaction of derivatives of 2,3,4,5-tetrahydro-3-carboline with acid chlorides, we undertook the preparation of several bases of this group, including 3-methyl-2,3,4,5-tetrahydro-3-carboline (also known as N-methyltetrahydronorharmane) (I):

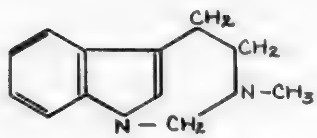


(I)

Having acquired a sufficient supply of N-methyltryptamine, we naturally determined to prepare the above-mentioned compound via the condensation of N-methyltryptamine with formaldehyde by analogy with the well-known method of preparing other derivatives of 2,3,4,5-tetrahydro-3-carboline and also of tetrahydroisoquinoline.

In the condensation, which we brought about under the conditions described by Akabori [1], we completely unexpectedly obtained, however, a mixture of three bases, two of which had the elementary composition and molecular weight which corresponded to those of N-methyltetrahydronorharmane, i.e., $C_{12}H_{14}N_2$, and the third, to those of the empirical formula $C_{13}H_{16}ON_2$. In the investigation of the properties of the bases obtained, it turned out that both isomeric $C_{12}H_{14}N_2$ compounds were monoacidic bases, and the nitrogen atom, to which the basic properties were due, was of a tertiary nature and was included in the ring, since in a Hofmann degradation of the iodomethylates of both bases, the trimethylamine was formed only in the second stage. The two isomers were markedly different in the fact that one of them, the isomer with a m.p. of 225-226°, was incapable of reacting with nitrous acid, while the other (with a m.p. of 217-218°) yielded a nitrosocompound but, however, retained a basic character and on heating with acids was readily reconverted into the initial substance. This observation permitted the solution of the problem of determining which of the two isomeric bases was N-methyltetrahydronorharmane (I), in favor of the base with a m.p. of 217-218°.

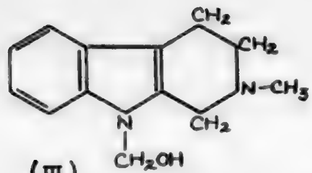
For the second isomer with a m.p. of 225-226°, formula (II) seemed uniquely possible to us, since it satisfactorily explained not only the properties of this compound



which had been described befoe, but also the fact that it is formed in the condensation of N-methyltryptamine with formaldehyde.

The structure of the third compound of composition $C_{13}H_{16}ON_2$ was established on the basis of the observation that on heating the base above its melting point, the substance splits off a molecule of formaldehyde and is converted into a base with a m.p. of 217-218° which proved to be identical with N-methyltetrahydronorharmane (I). This behavior of the base with the composition $C_{13}H_{16}ON_2$ is readily explained by formula (III):

* Deceased.



(III)

We assumed that this last substance (1-hydroxymethyl-3-methyl-2,3,4,5-tetrahydro-3-carboline or alternatively N(py)-methyl-N(ind)-hydroxymethyltetrahydronorharmane) is a secondary product of the reaction and, specifically, can be formed only in the presence of a sufficient excess of formaldehyde via the condensation of N-methyltetrahydronorharmane with a new molecule of formaldehyde. It consequently, seemed to us to be not without interest to investigate how the yield of condensation products changes depending on the quantity of formaldehyde taken for the reaction. The results, which completely confirmed our assumptions, are presented in the table.

The marked reduction in the yield of product (II) when the quantity of formaldehyde is equivalent to the theoretical amount, is not entirely clear.

TABLE

Quantity of moles of formaldehyde per mole of N-methyltryptamine	Yield (%)		
	N-methyltetrahydronorharmane (I)	N(py)-methyl-N(ind)-hydroxymethyltetrahydronorharmane (III)	Base (II)
6	–	57	14
2	23	41	12
1	78	–	2

It seems possible to us to explain the cause of the lowered yield of 2,3,4,5-tetrahydro-3-carboline in the condensation of tryptamine with formaldehyde in the case of an excess of the latter as Spӓth reports concerning this [2], in connection with the results obtained.

Tetrahydronorharmane, which has, in comparison with N-methyltetrahydronorharmane, not only an extra, but also more active hydrogen atoms, naturally exhibits to a much greater extent a tendency toward the formation of secondary condensation products in the presence of the excess aldehyde which, on account of side reactions, is ordinarily taken in a quantity several times greater than is theoretically required.

EXPERIMENTAL

17 ml of H_2O and 8 ml of a 35% solution of formalin (2.8 g of the aldehyde) was added to a solution of 8 g of N-methyltryptamine in 95.1 ml of 0.5 N H_2SO_4. The solution was slowly heated on an oil bath to 110° and this temperature was maintained for 20 minutes. The cooled solution was rendered alkaline with KOH, extracted with chloroform and the chloroform extract treated with 10% H_2SO_4.

After the addition of excess alkali to the acid solution, the base was extracted with ether. 3 fractions of crystals with m.p. of 208-211, 180-188 and 133-136° were isolated from the ethereal solution by fractional crystallization. Two bases were isolated from the first two fractions by repeated recrystallization from acetone, or better, from a mixture of benzene and alcohol; one of these, obtained in the form of fluffy flakes and needles, had a m.p. of 217-218° (2 g), while the other, consisting of prisms (1.02 g) melted at 225-226°. Both bases were completely colorless and poorly soluble in ether, alcohol and acetone; they were not soluble in water.

A base with a m.p. of 140-141° (prisms, 4.1 g) was isolated from the third fraction of crystals with a m.p. of 133-137° by recrystallization from ether, and proved to be the chief constituent part of this fraction.

Base with a M.p. of 217-218° (I)

0.0742, 0.0702 g sub.: 0.2104, 0.1986 g CO_2; 0.0498, 0.0484 g H_2O. 0.0664, 0.0738 g sub.: 8.85 ml N_2 (17.5°, 753 mm); 9.8 ml N_2 (17.5°, 751 mm). 0.0144 g sub.: 20.1072 g benzene: Δt 0.020° (average of 3 determinations). 0.0196 g sub.: 0.2282 g camphor: Δt 20.5°. Found %: C 77.35, 77.15; H 7.51, 7.73; N 15.2, 15.11; M 183 (by Beckmann's method), 167.5 (by Rast's method). $C_{12}H_{14}N_2$. Calculated %: C 77.36; H 7.58; N 15.05; M 186.

Hydrochloride. It was prepared by dissolving the base in an alcoholic solution of HCl. After adding a small quantity of ether, crystals were rapidly formed in the form of fine, snow-white needles with a m.p. of 247-248°.

Picrates. Depending on the quantity of picric acid, either the yellow mono-, or the red dipicrate can be obtained. The latter crystallizes (from alcohol) only in the presence of a large excess of picric acid, and when it is recrystallized in the absence of free picric acid, a mixture of the mono- and dipicrates crystallizes out. The melting point of the dipicrate is 175-176°, of the monopicrate, 195-196°. A mixed sample melted at 155-165°.

Analysis of the dipicrate with a m.p. of 175-176°: 0.0832, 0.0904 g sub.: 0.1362, 0.1478 g CO_2; 0.0228, 0.0258 g H_2O. Found %: C 44.64, 44.59; H 3.06, 3.19. $C_{12}H_{14}N_2 \cdot (C_6H_3O_7N_3)_2$. Calculated %: C 44.7; H 3.12.

Nitroso compound. A 10% nitrite solution was gradually added to 0.2 g of the base in 5% H_2SO_4 while it was being cooled. The solution thereupon became yellow, but remained transparent. After the addition of excess alkali, the yellow precipitate which settled out was treated with ether and the ethereal solution was concentrated. A yellow oil remained in the residue which clearly reproduced the Liebermann reaction and was quite soluble in acids. The nitroso product obtained was dissolved in 5 ml of acetone and converted into the picrate by the addition of an acetone solution of picric acid. Almost at once the crystallization of the picrate began; the picrate was poorly soluble in cold acetone. The decomposition temperature was 210-211° (it preliminarily darkened and shrank at about 196-197°). The picrate reproduced the Liebermann reaction. On heating the alcoholic solution of the picrate with excess picric acid, the solution reddened, and after cooling, the dipicrate of the initial base crystallized out.

Analysis of the picrate with a decomposition temperature of 210-211°: 0.0766 g sub.: 12.8 ml N_2 (19°, 757 mm). Found %: N 19.03. $C_{12}H_{13}N_2NO \cdot (C_6H_3O_7N_3)$. Calculated %: N 18.92.

Iodomethylate. 0.4 g of the base was dissolved in a mixture of 10 ml of methanol and 1 ml of CH_3I. The iodomethylate thereupon quickly began to crystallize; after recrystallization from methanol it had a m.p. of 257-258°. The yield was 0.67 g.

Hofmann degradation of the iodomethylate. A solution of 0.6 g of the iodomethylate and 5 g of KOH in 35 ml of methanol was heated for 5 hours on a water bath. The evolution of trimethylamine was not observed. The methyl alcohol was driven off on a water bath and the residue was treated with ether. After eliminating the ether, the degraded base was left in the form of a yellow oil. The iodomethylate obtained from it in the usual way, in contrast to the initial iodomethylate, was quite soluble in methanol. On heating the iodomethylate of the degraded base in an alcoholic KOH solution, the odor of trimethylamine quickly became clearly perceptible.

Base with a M.p. of 225-226° (II)

0.0930, 0.0724 g sub.: 0.2630, 0.2054 g CO_2; 0.0618, 0.0484 g H_2O. 0.0848, 0.0816 g sub.: 10.95 ml N_2 (17°, 770 mm), 10.7 ml N_2 (18°, 768 mm). 0.0252 g sub.: 20.2586 g benzene: Δt 0.033° (average of 3 determinations). 0.0062 g sub.: 0.1476 g camphor: Δt 9.5°. Found %: C 77.13, 77.37; H 7.43, 7.47; N 15.09, 15.23; M 193 (by Beckmann's method), 177 (by Rast's method). $C_{12}H_{14}N_2$. Calculated %: C 77.36; H 7.58; N 15.05; M 186.

Picrate. Upon addition of picric acid to a solution of the base in acetone, a crystalline yellow precipitate of the picrate at once settled out, which was very poorly soluble in the usual organic solvents and almost completely insoluble in water. The m.p. was 237-238°. The same picrate was formed in the presence of insufficient picric acid, as in the presence of a large excess of it.

Picrolonate. It consisted of a finely crystalline yellow precipitate which was very poorly soluble even in hot acetone; decomposition temperature, 223°.

Iodomethylate. 0.3 g of the base was dissolved in a mixture of 10 ml of methanol and 1 ml of methyl iodide; the crystallization of the iodomethylate in the form of clumps of fine needles, which were very poorly soluble in alcohol, thereupon quickly began; the m.p. was 272-273° (with decomposition).

Hofmann degradation of the iodomethylate. 0.3 g of the iodomethylate together with 40 ml of a 15% solution of KOH in methanol was heated for 8 hours on a water bath. The odor of trimethylamine was not perceived. The degraded base which was isolated by direct extraction with ether was converted into the iodomethylate; the latter gradually darkened on heating and at 187-188° became completely black. Further increase in the temperature even to 250° did not cause an appreciable change in the substance. On heating the iodomethylate of the degraded base in an alcoholic solution of potassium hydroxide, the odor of trimethylamine was quickly clearly perceptible. After heating for 6 hours, the methyl alcohol was driven off, and the residue was diluted with water and subjected to extraction with ether. The ethereal solution was shaken with a 2% solution of H_2SO_4 and then dried with potash. The residue after the ether had been eliminated quickly crystallized out. The substance obtained,

neutral to litmus, was poorly soluble in alcohol and quite soluble in benzene. The m.p. was 151-152°. It reproduced the Ehrlich reaction, but only on heating. As a consequence of the insufficient amount of the substance, the elementary analysis was not carried out.

Attempt at nitrosation. Nitrite solution was gradually added to an ice-cooled solution of 0.2 g of the base in 5% H_2SO_4. The liquid remained transparent under these conditions. After the solution had been rendered alkaline, the product was extracted with ether and proved to be the initial base.

Base with a M.p. of 140-141° (III)

0.0962, 0.0834 g sub.: 0.2550, 0.2206 g CO_2; 0.0652, 0.0556 g H_2O. 0.0992, 0.0978 g sub.: 11.4 ml N_2 (18°, 751 mm), 11.35 ml N_2 (18°, 751 mm). Found %: C 72.28, 72.14; H 7.58; 7.46; N 13.05, 13.18. $C_{13}H_{16}ON_2$. Calculated %: C 72.18; H 7.46; N 12.96.

Hydrochloride. After the base had been dissolved in an alcoholic HCl solution, crystallization of the hydrochloride began almost at once; it was poorly soluble in cold alcohol. The m.p. was 198° (with decomposition).

Picrate. It consisted of yellow needles which were very poorly soluble in alcohol and melted at 191-192°.

The base dissolved quite well in the usual organic solvents. When the base was fused, the evolution of gas bubbles occurred, after which the substance once more hardened and melted again at 211-213°.

With the object of elucidating the chemistry of this conversion, 0.3 g of the base was heated to 160° for 5 minutes in a test tube on an oil bath. The gaseous substance which was evolved during the heating proved to be formaldehyde, the sharp odor of which was perceived only a few seconds after the beginning of the heating. The thickening substance melted at 217-218° after recrystallization from acetone. The substance proved to be identical with the base which had a m.p. of 217-218°. A mixed sample melted at the same temperature.

Experiments involving the condensation of N-methyltryptamine with the theoretical, and with a six-fold, quantity of formaldehyde were carried out under conditions which were analogous to those described above. The yields of the separate condensation products are presented in the table which appears in the theoretical part of this article.

SUMMARY

1. In the reaction of N-methyltryptamine with formaldehyde, in addition to the fundamental reaction which leads to the synthesis of 3-methyl-2,3,4,5-tetrahydro-3-carboline, there also occurs the condensation of a formaldehyde molecule with the two nitrogen atoms of N-methyltryptamine with the formation of a seven-membered ring.

2. In the presence of excess formaldehyde, the 3-methyl-2,3,4,5-tetrahydro-3-carboline, in adding a second molecule of formaldehyde, is converted into 1-hydroxymethyl-3-methyl-2,3,4,5-tetrahydro-3-carboline.

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INVESTIGATION OF THE DELPHINIUM ALKALOIDS

VI. THE N-ALKYL GROUP OF DELSINE

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As is well-known, one of the characteristic peculiarities of the aconitic alkaloids consists in the fact that to a considerable extent their nitrogen is alkylated with the ethyl radical. Several years ago, this interesting fact was almost simultaneously noted by three groups of investigators [1, 2, 3], and although it subsequently was the basis of many works on the aconitines, it, however, still remains disputable.

The character of the N-alkyl group in the aconitine series of alkaloids is judged by the following signs:

a) When the alkaloid is fused with alkalis, methylamine or ethylamine is,respectively, detected in the volatile products of dry distillation which are characterized most simply by the picrates [1, 2, 3];

b) In a well-known method of determining the alkoxy and alkylimide groups, when they are both present, the methoxy groups of the alkaloid are initially saponified with hydriodic acid, and then the alkyl group is split off from the nitrogen; the alkyl iodide formed is trapped with a trimethylamine solution and identified in the form of the iodide of tetramethylammonium or triethylammonium [1, 2, 3].

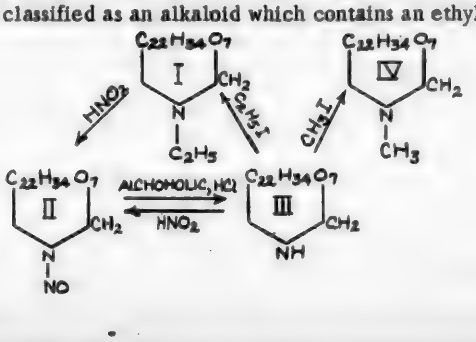
c) When oxidized with permanganate in sulfuric acid solution the aconitine alkaloids, depending on the character of the N-alkyl group, split off formaldehyde or acetaldehyde; either of these aldehydes is readily determined in the form of the condensation product with dimedone [3, 4, 6].

It is not difficult to see that the methods indicated above, in spite of their apparent objectivity, are also not free of substantial defects. Thus, alkyl iodides and alkylamines are products of the pyrogenetic reactions which are brought about at 250-300°, and can prove to be fragments of the more important portions of the molecule. In exactly the same way, the source of the aldehydes can equally be a different kind of C-alkyl grouping.

Actually, in the alkaline cleavage of aconitine, along with ethylamine, a small quantity of methylamine [3] is always formed. Demethylated aconitine [2] and isoatisine [5], under conditions which are appropriate for the determination of an N-alkyl group, yield a mixture which consists of ethyl iodide and an appreciable quantity of methyl iodide. In certain oxo-derivatives, the alkylimidic group in general does not submit even to qualitative determination [7, 8, 9]. It is, consequently, not accidental that the question of the character of the N-alkyl group of the aconitines has remained in dispute up to the present time [10]. Not only the presence of an N-ethyl group, but in general, the very presence of any alkyl group on the nitrogen atom, has been questioned [7,9]. It is assumed that "it is possible that the so-called N-alkyl group is actually only a rather labile C-alkyl group", or "this alkyl group acts as a connecting link between the nitrogen atom and the rest of the molecule" [8]. Finally, Jacobs [11] recently expressed the opinion that the nitrogen in atisine is alkylated with a hydroxyethyl group $>N-CH_2-CH_2OH$. No experimental data in support of this hypothesis were adduced.

Since many questions are closely linked with the character of the N-alkyl group, which concern the structure of the series of alkaloids under consideration, we have undertaken several new investigations in this direction.

As has already been described [12], to elucidate the attachment of the N-alkyl group of the alkaloid delsine, the latter was subjected to oxidation with potassium permanganate; acetaldehyde was thereupon detected, on the basis of which delsine was classified as an alkaloid which contains an ethyl group on the nitrogen. Experimental



data are cited in the present article, which completely confirms this hypothesis.

We have succeeded in bringing about the partial cleavage and resynthesis of the alkaloid. Under the oxidizing action of excess nitrous acid, the nitrogen alkyl group was eliminated from delsin , which led to the formation of the nitroso compound (II). The product obtained by reduction in an alcoholic solution of hydrochloric acid was converted into the free nor-base (III). The secondary character of base (III) was confirmed by the fact that it readily yields back the initial nitroso compound (II) with dilute nitrous acid. The nor-base of delsine was in turn alkylated with methyl iodide and ethyl iodide. The product of the first reaction (IV) proved to be distinct in its physico-chemical constants from delsine. A compound which was completely identical with the hydriodide of delsine was obtained by alkylating the nor-base with ethyl iodide.

A special experiment was set up to elucidate the character of the oxidizing action of potassium permanganate on nordelsine. As was not strange, even without an alkyl group at the nitrogen, the base proved to be still capable of splitting off aldehyde, although this time, for some reason, it is formaldehyde. It is necessary to assume that the fact, which has long been well-known, that aldehydes are formed in the oxidation of aconitine alkaloids is evidently associated not only with the presence of alkylated nitrogen atoms, but also with the presence of other elements making up the structure of the molecule which readily yield to oxidation.

In the first communication on the discovery of delsine [12], the reservation was made that this alkaloid in certain of its properties resembles the amino alcohol lycotonine, but differs from it in the character of the substituent groups and the melting points of its salts. Several new works on lycotonine have appeared in subsequent years [10, 13, 14, 15]. The corrected constants of lycotonine are identical in the majority of cases with the data previously indicated by us for delsine. The formula $C_{25}H_{41}O_7N \cdot H_2O$ is also acknowledged as the most reliable [10]. At the present time there remains almost no doubt relative to the identity of both bases. The presence of lycotonine – delsine has been definitely established in 9 forms of Delphinium (D. ajacis, D. barbeyi, D. brownii, D. consolida, D. elatum, D. oreophilum, D. rotundifolium, D. semibarbatum, D. sp) and only in one of the species of Aconitum (A. lycoctonum). Evidently, this is one of the most widely distributed alkaloids among the plants of the genus Delphinium; consequently, the name "delsine" more fully reflects the generic relation of the alkaloid with the plants which produce it. For this reason, the name "delsemidine" should be preferred to the name "methyllycaconitine".

EXPERIMENTAL

N-Nitrosonordelsine

Preparation. 10.0 g of delsine was dissolved in 400 ml of 25% acetic acid and heated on a water bath. 100 ml of a 60% solution of sodium nitrite was separately prepared. The nitrite was introduced into the reaction mixture in equal portions of 25 ml: the first portion at once, the other portions at 15 minute intervals. After the last portion had been added, the heating was continued for 1 hour more. The cooled solution was neutralized with sodium carbonate and extracted with chloroform. The chloroform solution was concentrated to small volume. The residue was freed from the chloroform by subsequent concentration in air of alcohol and water solutions. After 2-3 days in a concentrated water solution, a crystalline precipitate of nitrosonordelsine began to settle out. The yield was 2.1 g. The bulk of the alkaloid which had reacted was left in the water-alkali solution in the form of an amphoteric compound. The latter displayed a positive reaction with silicotungstic acid, but did not dissolve in organic solvents.

In another experiment a solution of 4.0 g of delsine in 160 ml of 5% sulfuric acid was treated under analogous conditions with 40 ml of a 30% solution of $NaNO_2$. As a result, 2.6 g of delsine was recovered and only 0.25 g of nitrosonordelsine was isolated. We did not succeed in increasing the yield of the nitroso product above 20-22%.

Properties. For recrystallization, the nitroso compound was dissolved in a small quantity of alcohol; the solution was diluted with water and slowly concentrated in air. After it had been twice recrystallized in a similar fashion, the substance formed long, colorless, needle-like crystals with a m.p. of 79-80°* $[\alpha]_D^{16}$ −50.7° (c 2.38 in ethanol). On heating, and also on standing in a vacuum desiccator over $CaCl_2$, the crystals acquired a dull tinge, which was associated with the loss of four molecules of water of crystallization.

Found %: H_2O 13.44, 13.61. $C_{23}H_{36}O_8N_2 \cdot 4H_2O$. Calculated %: H_2O 13.33.

The dried product had no sharp melting point. It began to sinter at 124°, and the substance finally softened at 128°, but even at 135° no clear meniscus was yet observable: $[\alpha]_D^{16}$ −59.5° (c 2.00 in ethanol).

Found %: C 58.68, 58.72; H 7.92, 7.79; N 5.87, 5.92; OCH_3 26.28, 26.36. $C_{23}H_{36}O_8N_2$. Calculated %: C 58.96; H 7.74; N 5.98; $4OCH_3$ 26.49.

* All the melting points given in the text are corrected.

The analysis for methoxy groups was hampered due to the instantaneous evolution of iodine. The substance showed an appreciable reaction for the nitroso group with phenol and sulfuric acid. The nitrosonordelsine was not precipitated from acidified solutions by silicotungstic acid, although it still retained certain weakly basic properties.

The hydrobromide of nitrosonordelsine was isolated in the form of coarse prisms by adding dry ether to an alcoholic solution of the nitroso product which was acidified with hydrobromic acid. After recrystallization from a mixture of alcohol and ether, it had a m.p. of 187-188° (decomposition).

The chlorate of nitrosonordelsine was precipitated in an analogous fashion with ether from an alcoholic solution of the nitroso compound which was acidified with chloric acid. The dried salt melted at 188° (with decomposition).

A small quantity of the salt was treated with ammonia and the nitrosamine which was freed was extracted with chloroform. The chloroform was evaporated off, and the residue was recrystallized from water. The crystals thereby obtained had a m.p. of 77-79° and a mixed sample with nitrosonordelsine displayed no melting point depression.

Nordelsine

Preparation. The nitrosamine was not reduced in the presence of platinum black either in alcoholic or in acetic acid solution, even when the temperature was raised.

1.75 g of the anhydrous nitrosonordelsine was dissolved in 25 ml of anhydrous alcohol, and the solution was saturated with hydrogen chloride while being cooled externally to −10°. The reaction mixture was kept for 3 days in a sealed tube at room temperature, and then was concentrated in a vacuum. The residue was dissolved in 20 ml of water and after neutralization (to the point at which gas bubbles were no longer evolved) with sodium carbonate, it was repeatedly extracted with chloroform (for the neutral reaction products). The aqueous solution was then rendered strongly alkaline with ammonia, and the basic reaction products were extracted with chloroform. The chloroform solution was concentrated to small volume. At the end, several milliliters of water were added to the flask to be distilled off, and the heating was continued until no chloroform odor was present and the reaction product did not dissolve in water. The aqueous solution was filtered and concentrated on a water bath. The residue was dried in a vacuum desiccator over calcium chloride. The yield of nor-base was 1.16 g.

The chloroform solution which contained the neutral reaction products was treated in exactly the same way and gave 0.36 g of a brownish amorphous mass.

Properties. Nordelsine consists of a vitreous substance of a yellowish color, and is readily converted into an amorphous powder on grinding. It is quite soluble in water. We did not succeed in crystallizing the base from any solvent or in obtaining its crystalline salts. Nordelsine begins to sinter at approximately 80° and melts at 102-104°; $[\alpha]_D^{25}$ + 54.1° (c 5.19 in ethanol for the dehydrated substance). The substance attracts moisture in air which is eliminated without difficulty in a vacuum. One molecule of water, however, is strongly held by the base and is evolved with foaming only at the melting point.

Found %: C 62.65, 62.57; H 8.64, 8.71; N 3.24, 3.31; H_2O 4.24. $C_{23}H_{37}O_7N$. Calculated %: C 62.85; H 8.48; N 3.19; H_2O 3.94.

Nordelsine and HNO_2. 0.2 g of nordelsine was dissolved in 10 ml of 10% sulfuric acid and treated with 3 ml of a saturated solution of sodium nitrite. The reaction mixture was left for a day at room temperature. On the following day, the solution was rendered alkaline with ammonia and extracted with chloroform. The chloroform was driven off and the residue (0.17 g) was twice recrystallized from water. The crystals obtained, with a m.p. of 79-80°, $[\alpha]_D^{16}$ −51.3° (c 2.02 in ethanol), were completely identical with nitrosonordelsine.

Oxidation of nordelsine. 0.40 g of $KMnO_4$ in 10 ml of water was added over a period of 2 hours to a cooled solution of 0.41 g of nordelsine in 10 ml of 5% sulfuric acid which was being stirred. After the solution had become colorless, the manganese dioxide precipitate was filtered off, and the filtrate was distilled into a well-cooled receiving vessel. 20 ml of a 1% aqueous solution of dimedon was added to the distillate obtained, which had an acid reaction. The mixture was heated for several minutes on a boiling water bath; turbidity thereupon appeared which was converted into a finely crystalline precipitate. The yield was 12 mg. After recrystallization from dilute alcohol, the crystals had a m.p. of 188°. A mixed sample with the product of the condensation of dimedon with formaldehyde melted at 187-188°.

N-Methylnordelsine

Preparation. 0.55 g of nordelsine was dissolved in 8 ml of methanol, stirred with 0.5 ml of methyl iodide and heated in a sealed tube on a water bath for 2 hours. The excess of methyl iodide and methanol was evaporated

off and the solution concentrated to small volume (1.5-2 ml). Ether (6-8 ml) was poured into the cooled solution along the walls. After some time, needle-like crystals of methyl-nordelsine hydriodide began to grow at the boundary of the two layers. The salt obtained was dissolved in 25 ml of water, the solution filtered and rendered alkaline with ammonia. On long standing, the N-methylnordelsine crystallized out in the form of coarse truncated tetrahedra. The yield was 0.37 g. The crystallization of the methylated base was considerably facilitated if the iodine ion was preliminarily precipitated from the solution with the aid of the calculated quantity of silver oxide.

Properties. After recrystallization from dilute alcohol, the N-methylnordelsine was in the form of the crystalline hydrate which contains 4 molecules of water.

Found %: H_2O 13.83. $C_{24}H_{39}O_7N \cdot 4H_2O$. Calculated %: H_2O 13.71.

The melting point of the base depends on the quantity of solvent of crystallization. The crystalline hydrate, with 4 molecules of water, melts at 106-108° with vigorous foaming, $[\alpha]_D^{22}$ + 46.9° (c 0.64 in ethanol). The substance, dried at 40-50° or in a vacuum dessiccator over calcium chloride at room temperature, loses 3 molecules of water and then has a m.p. of 130-131°, $[\alpha]_D^{25}$ + 52.5° (c 3.00 in ethanol). The compound completely dried at 100-110° does not have a crystalline structure and melts over a wide range between 85 and 98°; $[\alpha]_D^{25}$ + 54.6° (c 3.13 in ethanol).

Found %: C 61.01, 60.93; H 8.79, 8.83; N 3.05, 3.11; OCH_3 26.39, 26.25. $C_{24}H_{39}O_7N \cdot H_2O$. Calculated %: C 61.12; H 8.76; N 2.97; $4OCH_3$ 26.33.

The hydrobromide of N-methylnordelsine was precipitated with dry ether from a solution of 70 mg of the base in 0.2 ml of methanol which had been acidified with hydrobromic acid. After recrystallization from alcohol-ether, the dried salt melted rather sharply at 199° (with decomposition).

The hydriodide of N-methylnordelsine was prepared analogously from a solution of 50 mg of the base in 0.2 ml of alcohol which was acidified with colorless hydriodic acid. The salt, after having been recrystallized and dried at 105° in a vacuum, had a m.p. of 204-205° (with decomposition).

Perchlorate of N-methylnordelsine. 60 mg of the base was dissolved in 0.2 ml of methanol, and 60 mg of magnesium perchlorate and a drop of hydrochloric acid (until the reaction was acid to Congo red) were then added. Ether was added from above. After some time, crystals of the perchlorate of N-methylnordelsine began to precipitate at the boundary of the two solvents. The salt, after having been twice recrystallized from a mixture of alcohol and ether and dried at 100°, sintered at 183° and melted at 187-188° (with decomposition).

N-Ethylnordelsine

Preparation. 0.30 g of nordelsine was dissolved in 5 ml of ethanol, stirred with 0.5 ml of ethyl iodide and heated in a sealed tube on a water bath for 2 hours. The excess of ethyl iodide and ethanol was evaporated off and the solution concentrated to small volume. Ether was added to the residue. Rapidly accelerating crystallization began at once. The salt which precipitated was separated and dissolved in 2 ml of water. The aqueous solution was rendered alkaline with ammonia. The contents of the vessel were quickly filled compactly with fine silky threads of N-ethylnordelsine. After recrystallization from dilute alcohol, the alkylated base melted with foaming at 138-139°, $[\alpha]_D^{25}$ + 50.0° (c 0.80 in ethanol).

A mixed sample of the N-ethylnordelsine with an original sample of delsine displayed no melting point depression. When dried in a vacuum, the resynthesized base, similarly to the initial alkaloid, lost a molecule of water of crystallization and forms an amorphous substance $[\alpha]_D^{22}$ + 52.4° (c 0.91 in ethanol).

The hydrohalides of N-ethylnordelsine were prepared in exactly the same way as was indicated for delsine [12]. The hydrobromide of the resynthesized base melted at 183-184°, the hydriodide melted at 187°. Mixed samples of these salts with the salts of delsine displayed no melting point depression or depression of the decomposition temperature.

The perchlorate of the base was prepared by analogy with the perchlorate of N-methylnordelsine. It had a m.p. of 215° and was completely identical in its properties with the perchlorate of the natural delsine.*

Found %: C 61.62; H 9.01; N 2.94; OCH_3 25.25. $C_{25}H_{41}O_7N \cdot H_2O$. Calculated %: C 61.83; H 8.93; N 2.88; $4OCH_3$ 25.56.

* In one of the preceding communications [12], the chlorate of delsine, $C_{25}H_{41}O_7N \cdot HClO_3$, which has a m.p. of 145-146°, was erroneously described as the perchlorate. It should be noted, that chloric acid in certain cases is one of the most convenient salt-forming reagents for the aconitine alkaloids and ordinarily gives anhydrous crystalline salts with well-expressed melting points.

SUMMARY

1. The conversion of delsine via the nitroso compound to the nor-base was accomplished. The alkylation of the latter with ethyl iodide gives a compound which is identical with the hydriodide of natural delsine.

2. The indicated series of conversions conclusively demonstrated the presence of an N-ethyl group in aconitine alkaloids.

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* See Consultants Bureau Translation, page 189.

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CHARACTERIZATION OF THE COMPOSITION OF THE ALKALOIDS OF DELPHINIUM ELATUM L.

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33 alkaloids from the genus Delphinium have been isolated and described in the literature which are close in their structure to the alkaloids isolated from plants of the genus Aconitum and constitute the single general group of aconitic alkaloids. A voluminous literature has been devoted to the investigation of the aconitic alkaloids. However, the chemical structure of these alkaloids has not been completely deciphered, which is explained by the exceptional complexity of their structure.

In the present work, we report the results of an investigation of an alkaloid which has not been previously described, which was obtained from the vegetable part of the "high larkspur" Delphinium elatum fam. Ranunculaceae, collected in the Altai Mountains in 1949 by the expedition headed by P. S. Massagetov. The entire aboveground portion of the plant, the alkaloid content of which amounted to 0.72% of the absolute dry weight, was subjected to investigation.

The total alkaloids obtained by the usual extraction of the vegetable portion with dichloroethane, were separated into 5 fractions, from which the fraction of weak bases, soluble in ether and present in comparatively maximum quantity in the alkaloid mixture, was taken for investigation. By a second conversion of the fraction into the salt and crystallization of the base from ether we succeeded in isolating a crystalline portion which, when dissolved in ethyl ether and precipitated with petroleum ether, crystallized in the form of triangular and hexagonal prisms. After 3-fold recrystallization, the base had a constant m.p. of 188-189°.

The alkaloid was quite soluble in chloroform, alcohol, ether and xylene; was insoluble in water and petroleum ether; and was optically active $[\alpha]_D^{17} - 36.84°$ (in anhydrous alcohol) and $[\alpha]_D^{17} - 26.32°$ (in chloroform). The following crystalline salts were prepared: the hydrochloride with a m.p. of 212-213° and the nitrate with a m.p. of 169-171°.

The empirical formula of the alkaloid — $C_{33}H_{47}O_9N$, which we called delphelatine — was established from the results of the elementary analysis of the base and its salts.

It became clear from the quantitative determination of the functional groups that 2 atoms of oxygen are found in the alkaloid in the form of hydroxy groups and 3 in the form of methoxy groups; the alkaloid is a tertiary base containing an N-alkyl (methyl?) group.

We present the partially expanded formula of the alkaloid:

$$C_{33}H_{47}O_9N \text{ or } C_{23}H_{28}O_2(NCH_3)(OCH_3)_3(OH)_2(OOCC_2H_5).$$

Delphelatine is an ester and is saponified by heating in a water-alcohol solution of alkali to give a crystalline amino alcohol which crystallized from ethanol in the form of coarse rectangular prisms, beveled at the corners, which melted at 235-237° and had the composition $C_{27}H_{43}O_8N$. The amino alcohol gives a crystalline hydrochloride $C_{27}H_{43}O_8N \cdot HCl$ with a m.p. of 222-223.5° and a nitrate $C_{27}H_{43}O_8N \cdot HNO_3$ with a m.p. of 199-200°. Determination of the functional groups in the amino alcohol showed the presence of three hydroxy groups; no methylenedihydroxy group was detected. We present the partially expanded formula of the amino alcohol:

$$C_{27}H_{43}O_8N \text{ or } C_{23}H_{28}O_2(NCH_3)(OCH_3)_3(OH)_3.$$

Rabinovich [1] studied the alkaloids of the vegetable parts of "high larkspur" simultaneously with us. It can be concluded from a comparison of the alkaloid eldeline described by the indicated author with the alkaloid delphelatine isolated by us (Table 1) that our base is not identical with eldeline, since it differs in composition, in the number of hydroxy groups and does not contain a methylenedihydroxy group, while this group is present in eldeline. In addition, when eldeline is saponified with alkali, it yields the amino alcohol eldelidine — $C_{25}H_{39}O_7N$ — and acetic acid; we obtained an amino alcohol with the composition $C_{27}H_{43}O_8N$, and an acid which is not acetic acid (Table 2).

TABLE 1

Property	Eldeline [1]		Delphelatine	
Base	M.p. 182-184°		M.p. 188-189°	
Formula of the base	$C_{27}H_{41}O_8N$		$C_{30}H_{47}O_9N$	
Percent composition:	Found:	Calculated:	Found:	Calculated:
Carbon	64.10, 63.82	63.91	63.49, 63.95, 63.68, 63.79	63.72
Hydrogen	8.12, 8.06	8.08	8.27, 8.48, 8.23, 8.37	8.32
Nitrogen	3.10, 2.78	2.76	2.59, 2.35, 2.38, 2.50, 2.47	2.48
Methoxy groups	18.27		18.24, 18.33, 18.30	
Hydroxy groups	3.55		5.64, 5.18, 5.74	
Methylenedihydroxy group	Present		Absent	
Hydrochloride of the base	M.p. 204-206° (decomp.)		M.p. 212-213° (decomp.)	
Nitrate of the base	M.p. 170-173°(decomp.)		M.p. 169-171° (decomp.)	
Percent content of nitrogen	Found:	Calculated:	Found:	Calculated:
	5.16, 5.20	4.91	4.72, 4.67	4.46

TABLE 2

Property	Eldelidine [1]		Amino alcohol, obtained by saponification of delphelatine	
Base	M.p. 226-228°		M.p. 235-237°	
Formula of the base	$C_{25}H_{39}O_7N$		$C_{27}H_{43}O_8N$	
Percent composition:	Found	Calculated:	Found:	Calculated:
Carbon	64.52, 64.39	64.52	64.07, 64.37, 64.17	63.91
Hydrogen	8.46, 8.47	8.38	8.48, 8.42, 8.36	8.08
Nitrogen	3.19, 3.24	3.01	2.79, 2.93, 2.72	2.76
Hydroxy groups	7.74		9.60, 10.25, 9.79	
Methylenedihydroxy group	Present		Absent	
Hydrochloride of the base	M.p. 216-218° (decomp.)		M.p. 222-223.5° (decomp.)	
Nitrate of the base	M.p. 186-188° (decomp.)		M.p. 199-200° (decomp.)	
Percent content of nitrogen	Found:	Calculated:	Found:	Calculated:
	5.18, 5.19	5.33	4.86, 4.66	4.89

TABLE 3

Alkaloid	Portion of the plant studied	Empirical formula	M	$[\alpha]_D$	M.p.
Delpheline [2]	Seeds	$C_{25}H_{39}O_6N$	449	−25.8° (in chloroform)	227°
Delatine [2]	Seeds	$C_{19}H_{25}O_3N \cdot H_2O$	315 + H_2O	+ 13.5° (in 0.5 N HCl)	148
Methyllycaconitine [2]	Seeds	$C_{37}H_{48}O_{10}N_2 \cdot H_2O$	680 + H_2O 698	+ 49.1° (in anhydrous alcohol)	128
Delphelatine	Vegetable material	$C_{30}H_{47}O_9N$	565	−26.32° (in chloroform)	188-189

The chemical study of the seeds of "high larkspur" was carried out by the English investigator Goodson in 1943 [2]. The alkaloids described by him are presented in Table 3, in which the constants of the base isolated by us — delphelatine — are also given for comparison.

As a result of the comparison of the properties of the alkaloids described by Rabinovich and Goodson, and also of all the alkaloids from plants of this genus which have been described, it can be stated that the alkaloid isolated by us is distinct from the previously known alkaloids.

EXPERIMENTAL

The vegetable material (grass) in a quantity of 9.0 kg was moistened with 10% ammonia solution and the alkaloids were extracted with dichloroethane. The dichloroethane extract was treated in its turn with 10% sulfuric acid until the alkaloids were completely extracted. The combined sulfuric acid extracts were filtered, rendered alkaline with ammonia, and the alkaloids extracted with chloroform. The alkaloids were then extracted from the

chloroform with a 10% solution of hydrochloric acid. The hydrochloric acid solution obtained of the alkaloids was separated into 5 fractions in the following manner.

7.64 g of a fraction (I) of the hydrochlorides of the alkaloids which were soluble in chloroform was obtained by extracting the hydrochloric acid solution with chloroform.

After the aqueous hydrochloric acid solution had been extracted with chloroform, it was rendered alkaline with $NaHCO_3$ and extracted initially with ether and then with chloroform. Two more alkaloid fractions were obtained: 25.0 g of weak bases, soluble in ether (II), and 20.58 g of weak bases, soluble in chloroform (III).

After the mother liquor had been rendered alkaline with ammonia, the portion of strong bases remaining was extracted again, initially with ether, and then with chloroform. 2.0 g of bases which were soluble in ether (IV) and 1.96 g of bases which were soluble in chloroform (V) were obtained.

The weakly basic fraction of alkaloids (II) constituted the greater portion of the alkaloid mixture. It was the first taken for investigation.

Isolation of the Base Delphelatine

The weak base fraction (II) was dissolved in 5% sulfuric acid and after the solution had been rendered alkaline with a 25% ammonia solution, it was extracted with ether. The ethereal extracts were combined and carefully dried with roasted potash. Upon condensation of the ethereal solution, crystals were formed which had the form of triangular and hexagonal prisms. After 3-fold crystallization by dissolving it in ethyl ether and precipitation with petroleum ether, the substance was colorless and had a constant m.p. of 188-189°. The alkaloid was quite soluble in chloroform, alcohol, ether and xylene; it was insoluble in water and petroleum ether.

To demonstrate the homogeneity of the alkaloid obtained, it was dissolved in 5% H_2SO_4 and, during divided addition of alkali, was extracted with ether. Several fractions were thus obtained, the hydrochlorides of which had the same melting point.

1st fraction: hydrochloride m.p. 212-213°; 2nd fraction: hydrochloride m.p. 211-212°.

On the basis of the results of the elementary analysis, the formula $C_{30}H_{47}O_9N$ must be ascribed to the base being investigated.

8.817 mg sub.: 20.514 mg CO_2; 6.522 mg H_2O. 8.088 mg sub.: 18.955 mg CO_2; 6.134 mg H_2O. 5.017 mg sub.: 11.707 mg CO_2; 3.693 mg H_2O. 5.248 mg sub.: 12.268 mg CO_2; 3.929 mg H_2O. 17.032 mg sub.: 3.16 ml 0.01 N HCl (Kjeldahl). 17.157 mg sub.: 2.88 ml 0.01 N HCl. 14.632 mg sub.: 2.49 ml 0.01 N HCl. 7.944 mg sub.: 1.42 ml 0.01 N HCl. 8.662 mg sub.: 1.53 ml 0.01 N HCl. Found %: C 63.49, 63.95, 63.68, 63.79; H 8.27, 8.48, 8.23, 8.37; N 2.59, 2.35, 2.38, 2.50, 2.47. $C_{30}H_{47}O_9N$. Calculated %: C 63.72; H 8.32; N 2.48.

Determination of the molecular weight (of an equivalent) of the alkaloid by titration. By dissolving the alkaloid in excess 0.1 N H_2SO_4 solution and back titration with 0.1 N NaOH solution in the presence of the indicator methyl red, the following data were found:

0.1230 g sub.: 2.44 ml 0.1 N H_2SO_4. 0.1272 g sub.: 2.46 ml 0.1 N H_2SO_4. 0.1670 g sub.: 3.15 ml 0.1 N H_2SO_4. 0.1348 g sub.: 2.44 ml 0.1 N H_2SO_4. Found equiv.: 504, 517, 530, 552. $C_{30}H_{47}O_9N$. Calculated equiv.: 565.

Determination of the specific rotation:

0.2000 g substance in 10 ml alcohol (c 2.000, l 0.95 dm) α −0.7°; $[\alpha]_D^{17}$ −36.84° (in anhydrous alcohol). 0.2000 g substance in 10 ml chloroform (c 2.000, l 0.95 dm) α −0.5°; $[\alpha]_D^{17}$ −26.32° (in chloroform).

Determination of the hydroxy groups (by Tserevitinov's method):

8.760 mg sub.: 0.72 ml CH_4 (26°, 748.6 mm). 8.078 mg sub.: 0.61 ml CH_4 (26°, 748.6 mm). 9.175 mg sub.: 0.77 ml CH_4 (22°, 746.6 mm). Found %: OH 5.64, 5.18, 5.74. $C_{30}H_{45}O_7N(OH)_2$. Calculated %: OH 6.00.

Determination of the methoxy groups (by the method of Fibek and Brekher):

7.859 mg sub.: 13.88 ml 0.02 N $Na_2S_2O_3$. 8.124 mg sub.: 14.40 ml 0.2 N $Na_2S_2O_3$. 9.005 mg sub.: 15.94 ml 0.02 N $Na_2S_2O_3$. Found %: OCH_3 18.24, 18.33, 18.30. $C_{27}H_{38}O_6N(OCH_3)_3$. Calculated %: $(OCH_3)_3$ 16.46.

Determination of the alkyl group bound to the nitrogen:

7.696 mg sub.: 2.83 ml 0.02 N $Na_2S_2O_3$. 7.559 mg sub.: 3.03 ml 0.02 N $Na_2S_2O_3$. 7.945 mg sub.: 2.73 ml 0.02 N $Na_2S_2O_3$. Found %: CH_3 1.84, 2.00, 1.72. $C_{29}H_{44}O_9NCH_3$. Calculated CH_3 2.65.

Delphelatine Hydrochloride

Dry gaseous hydrogen chloride was passed into the ethereal solution of the alkaloid. The amorphous precipitate at once obtained gradually became crystalline.

The hydrochloride crystallized in the form of needles, had a m.p. of 212-213° and the composition $C_{30}H_{47}O_9N \cdot HCl$.

9.206 mg sub.: 1.42 ml 0.01 N HCl, (Kjeldahl). 8.369 mg sub.: 1.30 ml 0.01 N HCl. Found %: N 2.15, 2.17. $C_{40}H_{47}O_9N \cdot HCl$. Calculated %: N 2.32.

Delphelatine Nitrate

To a saturated solution of the base in anhydrous ether (preliminarily dried with metallic sodium and redistilled) concentrated nitric acid was added in drops (while the solution was being cooled with ice) until the reaction was weakly acid. A fine crystalline precipitate gradually settled out (tetrahedral crystal type). The precipitate was filtered off, carefully washed with ethyl ether and dried. The nitrate had a m.p. of 169-171° and the formula $C_{30}H_{47}O_9N \cdot HNO_3$.

8.212 mg sub.: 17.014 mg CO_2; 5.635 mg H_2O. 8.543 mg sub.: 17.735 mg CO_2; 5.911 mg H_2O. 7.977 mg sub.: 2.69 ml 0.01 N HCL (Kjeldahl). 7.700 mg sub.: 2.57 ml 0.01 N HCl. Found %: C 56.54, 56.65; H 7.67, 7.74; N 4.72, 4.67. $C_{30}H_{47}O_9N \cdot HNO_3$. Calculated %: C 57.32; H 7.64; N 4.46.

Thus, the data of the elementary analysis of the base, the complete analysis of the nitrate and hydrochloride of the base and the determination of the equivalent by titration lead to the same empirical formula $C_{30}H_{47}O_9N$.

Saponification of Delphelatine

1.4544 g of the alkaloid was dissolved in 7.5 ml of alcohol and 6.0 ml of 1 N NaOH was added to the solution; the reaction mixture was heated on a water bath for 3 hours, after which it was concentrated almost to dryness. The crystalline residue obtained was transferred to a filter, carefully washed with water and dried in a vacuum desiccator.

The amino alcohol was recrystallized from alcohol; the crystals had the form of rectangular prisms, beveled at the corners, a m.p. of 235-237° and the formula $C_{27}H_{43}O_8N$. The amino alcohol was quite soluble in chloroform and ether, was more difficultly soluble in alcohol and was insoluble in water.

7.606 mg sub.: 17.887 mg CO_2; 5.730 mg H_2O. 4.647 mg sub.: 10.962 mg CO_2; 3.473 mg H_2O. 5.299 mg sub.: 12.442 mg CO_2; 4.018 mg H_2O. 8.738 mg sub.: 1.70 ml 0.01 N HCl (Kjeldahl). 8.774 mg sub.: 1.82 ml 0.01 N HCl. 9.238 mg sub.: 1.82 ml 0.01 N HCl. Found %: C 64.17, 64.37, 64.07; H 8.42, 8.36, 8.48; N 2.72, 2.93, 2.78. $C_{27}H_{43}O_8N$. Calculated %: C 63.91; H 8.08; N 2.76.

Determination of the molecular weight (of an equivalent) of the amino alcohol by titration. By dissolving the base in excess 0.01 N HCl solution and back titration with 0.01 N NaOH solution in the presence of the indicator methyl red, the following data were found:

8.905 mg sub.: 2.12 ml 0.01 N HCl. 8.759 mg sub.: 1.98 ml 0.01 N HCl. 8.185 mg sub.: 1.86 ml 0.01 N HCl. Found equiv.: 420, 442, 440. $C_{27}H_{43}O_8N$. Calculated equiv.: 509.

Determination of the hydroxy groups in the amino alcohol (by Tserevitinov's method):

5.933 mg sub.: 0.87 ml CH_4 (22°, 752.2 mm). 5.571 mg sub.: 0.78 ml CH_4 (22°, 752.2 mm). 5.881 mg sub.: 0.80 ml CH_4 (19°, 752.3 mm). Found %: OH 10.25, 9.79, 9.60. $C_{27}H_{40}O_5N(OH)_3$. Calculated %: $(OH)_3$ 10.02.

Determination of the methylenedihydroxy group: 0.02 g of the alkaloid was dissolved by heating in 5 ml of phloroglucinol sulfuric acid (in a test tube).* 2 ml of concentrated sulfuric acid was added to the hot solution; the solution was stirred and heated on a boiling water bath for half an hour. The appearance of a red coloration and a flocculent precipitate was not observed, which indicates the absence of the methylenedihydroxy group.

* The phloroglucinol sulfuric acid was prepared by dissolving 1.5 g of phloroglucinol in a mixture of 75 g of water and 50 g of concentrated sulfuric acid by heating; the solution was then cooled and, after standing for many hours, was filtered.

Hydrochloride of the Amino Alcohol

Upon passing dry gaseous hydrogen chloride into an anhydrous ether solution of the amino alcohol, needle-like crystals of the hydrochloride of the amino alcohol precipitated, which were separated, carefully washed with ether and dried in a vacuum desiccator; the m.p. was 222-223.5° (with decomposition).

7.571 mg sub.: 1.32 ml 0.01 N HCl (Kjeldahl). 8.776 mg sub.: 1.60 ml 0.01 N HCl. Found %: N 2.44, 2.55. $C_{27}H_{43}O_8N \cdot HCl$. Calculated %: N 2.56.

Nitrate of the Amino Alcohol

To a saturated solution of the amino alcohol in anhydrous ether, concentrated nitric acid was added in drops until the reaction was weakly acid; an amorphous precipitate of the nitrate of the amino alcohol settled out, which crystallized on standing. The precipitate was filtered off, carefully washed with ethyl ether and dried. After drying in a vacuum desiccator, the nitrate melted at 199-200° (with decomposition).

4.757 mg sub.: 9.766 mg CO_2; 3.211 mg H_2O. 4.505 mg sub.: 9.282 mg CO_2; 3.038 mg H_2O. 8.667 mg sub.: 2.88 ml 0.01 N HCl (Kjeldahl). 6.305 mg sub.: 2.19 ml 0.01 N HCl. Found %: C 56.02, 56.22; H 7.55, 7.54; N 4.66, 4.86. $C_{27}H_{43}O_8N \cdot HNO_3$. Calculated %: C 56.64; H 7.69; N 4.89.

SUMMARY

1. The alkaloid delphelatine—$C_{30}H_{47}O_9N$ with a m.p. of 188-189°— was isolated from the vegetable material of "high larkspur" (Delphinium elatum) and characterized.

2. Its crystalline salts — the hydrochloride, $C_{30}H_{47}O_9N \cdot HCl$ with a m.p. of 212-213°, and the nitrate $C_{30}H_{47}O_9N \cdot HNO_3$ with a m.p. of 169-171° — were prepared.

3. The presence in the alkaloid of two hydroxy, three methoxy, and the N-alkyl groups was established.

4. The amino alcohol $C_{27}H_{43}O_8N$, with a m.p. of 235-237° was prepared by the saponification of delphelatine.

5. The crystalline salts of the amino alcohol — the hydrochloride, $C_{27}H_{43}O_8N \cdot HCl$ with a m.p. of 222-223.5°, and the nitrate $C_{27}H_{43}O_8N \cdot HNO_3$, with a m.p. of 199-200° — were prepared.

6. The partially expanded formula of delphelatine is as follows:

$$C_{23}H_{28}O_2(NCH_3)(OCH_3)_3(OH)_2(OOCC_2H_5).$$

7. The partially expanded formula of the amino alcohol of delphelatine is as follows:

$$C_{23}H_{28}O_2(NCH_3)(OCH_3)_3(OH)_3.$$

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* See Consultants Bureau Translation, page 1743.